Dissertation on

CLINICAL ANALYSIS OF
STEROID INDUCED GLAUCOMA

Submitted in partial fulfillment of requirements of

M.S. OPHTHALMOLOGY

BRANCH – III

REGIONAL INSTITUTE OF OPHTHALMOLOGY

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003.

THE TAMIL NADU

DR.M.G.R. MEDICAL UNIVERSITY,

CHENNAI.

APRIL 2012

CERTIFICATE

This is to certify that this dissertation entitled **"CLINICAL ANALYSIS OF STEROID INDUCED GLAUCOMA"** is a bonafide record of the research work done by **Dr. VIJAY KRISHNAN B,** Post Graduate in Regional Institute of Ophthalmology and Government Ophthalmic Hospital, Madras Medical College and Government General Hospital, Chennai–03, in partial fulfilment of the regulations laid down by the Tamil Nadu Dr. M.G.R. Medical University for the award of the degree Master of Surgery in Ophthalmology Branch III, under my guidance and Supervision during the academic years 2009 - 2012.

Dr. K. MARAGATHAM, M.S., D.O.
Chief of Glaucoma Services,
RIO-GOH,
Egmore, Chennai – 600 008.

Dr. K. VASANTHA, MS. FRCS
Director and Superintendent,
RIO – GOH,
Egmore, Chennai – 600 008.

Dr. V. KANAGASABAI, MD., Ph.D.,
Dean,
Madras Medical College,
and Government General Hospital,
Chennai – 600 003.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3
Telephone No: 04425305301
Fax : 04425363970

CERTIFICATE OF APPROVAL

To
Dr. B. Vijay Krishnan
PG in MS Ophthalmology
Madras Medical College, Chennai -3.

Dear B. Vijay Krishnan

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled "The Clinicoanalytical study in 50 patients of steroid induced glaucoma atregional Institute of Ophthalmology, Madras Medical college and Govt. Ophthalmic Hospital, Chennai " No. 23082011.

The following members of Ethics Committee were present in the meeting held on 16.08.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. V. Kanagasabai, MD Dean, Madras Medical College, Chennai-3,	-- Deputy Chairman
3.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
4.	Prof R. Sathianathan , MD	-- Member
5.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
6.	Prof. C. Rajendiran, MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
7.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
8.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
9 .	Tmt. Arnold Soulina MA	-- Social Scientist

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

ACKNOWLEDGEMENT

My sincere thanks and gratitude to **Prof.Dr.V.Kanagasabai** M.D. Ph.D. Dean Madras Medical College for permitting me to conduct this study at the Regional Institute of Ophthalmology, Government Ophthalmic Hospital, Chennai.

With profound gratitude I thank **Prof.Dr.K.Vasantha** M.S., FRCS, Director and superintendent, Regional Institute of Ophthalmology and Government Ophthalmic hospital Chennai, for her valuable advice and guidance throughout my post graduate course and her encouragement in preparing this dissertation.

I am forever grateful to **Prof.Dr.K.Maragatham** M.S., D.O. who with her unfathomable patience received my work and provided critical evaluation and support in analyzing the study.

I convey my heartfelt thanks to the assistant professors in my unit.

To **Dr.N.Sharmila** M.S. for being constant source of encouragement and support in all my endeavours

To **Dr.B.Kalaiselvi** M.S. for her constant source of cheer and encouragement.

To **Dr.R.Muthaiah** M.S. for his incessant help and support in conducting this study.

My sincere thanks to **Dr.Madhivanan Natarajan,** and **Dr.Chalini Madhivanan**, Directors M.N. Eye Hospital for permitting me to do selective laser trabeculoplasty in their hospital.

My heart felt thanks to **Dr.Murali Ariga** M.S. DNB visiting consultant M.N.Eye Hospitals for performing selective laser trabeculoplasty for 10 patients in my study.

My sincere thanks to all the assistant professors and my colleagues for their timely help and encouragement throughout my course in Ophthalmology.

Finally, I am greatly indebted to all my patients for their cooperation, who made this study possible.

CONTENTS

PART ONE

INTRODUCTION

Today glaucoma is the second most common cause of blindness. Glaucoma is the most common cause of irreversible blindness in the world. The world health organisation estimates (2002) that number of people who have become blind because of glaucoma were 4.4 million (12.3% of the blind world wide) population based studies have estimated that the prevalence of glaucoma in India to be about 11.9 million and 60.5 million in the world in 2010.

Glaucoma is defined as a disturbance of the structural or functional integrity of the optic nerve that can usually be arrested or diminished by adequate lowering of Intraocular pressure (IOP).[1]

Traditionally glaucoma has been classified as primary and secondary forms. Within this large group of glaucoma, primary open angle glaucoma is the most common form.

CLASSIFICATION OF GLAUCOMAS

The major classification of the glaucomas relates to the configuration of the anterior chamber angle and the age of onset of the disease. Glaucomas are classified in to:

1. **Open angle glaucoma -**

   a. Primary open angle glaucoma

   b. Normal tension glaucoma

   c. Juvenile glaucoma

   d. Ocular hypertension

   e. Secondary open angle glaucoma

2. **Angle closure glaucoma -**

   a. Primary angle closure glaucoma

   b. Secondary angle closure glaucoma either with or without pupillary block

3. **Childhood glaucoma -**

   a. Primary congenital or infantile glaucoma

   b. Glaucoma associated with congenital anomalies

   c. Secondary glaucoma in infants and children

Primary open angle glaucoma is explicitly characterised as multifactorial optic neuropathy with a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons developing in the presence of open anterior chamber angles and manifesting characteristic visual field abnormalities. Other types of glaucoma invariably the secondary glaucoma, historically even the

primary angle closure glaucoma are defined first and foremost by presence of elevated IOP[1,2]

A certain percentage of the general population responds to repeated instillation of systemic or ocular corticosteroid with a variable increase in IOP. The people who manifest this response to long term steroid therapy whether given by the topical, systemic, periocular or intra ocular route and IOP elevation can lead to glaucomatous optic atrophy and loss of vision. Such a condition is referred to as steroid induced glaucoma.[1,2]

SECONDARY OPEN ANGLE GLAUCOMA

1. Pigmentary glaucoma
2. Exfoliation syndrome
3. Corticosteroid glaucoma
4. Lens induced glaucoma
    a. Phacolytic glaucoma
    b. Lens particle glaucoma
    c. Phacoanaphylaxis

5. Glaucoma after cataract surgery

6. Glaucoma after trauma

7. Glaucoma associated with intraocular hemorrhage

8. Retinal detachment and glaucoma

9. Glaucoma after vitrectomy

10. Glaucoma with uveitis

11. Intra ocular tumors and glaucoma

12. Amyloidosis

13. Elevated episcleral venous pressure

Approximately 30% of the patients on topical therapy may be affected.25% responders of the general population respond to steroid and elevation in IOP after 4 weeks of usage of steroid, 5% of the population were high responders. They show 10 to 15 mm of Hg greater, may develop IOP rise within 2weeks.

HISTORICAL REVIEW

First case of steroid induced glaucoma was recognised by E.S.PERKINS in 1957. The patient was treated for chronic chorio retinal inflammatory disease with cortisone 25 mg daily for few months. IOP reduced after stopping steroids.

In 1954 cases of similar nature were noted by Francois. In 1955 Laval and Collier noted some cases of steroid induced glaucoma.

In 1958 Covell reported three cases of glaucoma occurring in patients receiving steroid therapy for arthritis.

In 1963 Becker and Mills showed local application of steroids can cause rise in IOP. In 1963 Armaly has suggested that cortisone known to have some effect on mucopolysaccharides and increase in resistance to outflow, which could be due to swelling of this layer, perhaps viscosity of this layer.[15,18,23]

In 1964 Becker and Hahn showed response to steroid had genetic basis

STAGES OF GLAUCOMA

STAGE : 1 initiating events

STAGE : 2 structural alterations

STAGE : 3 functional alterations

STAGE : 4 retinal ganglion cell and optic nerve damage

STAGE : 5 visual loss

STAGE : 1

Includes the condition or series of condition that sets in motion the chain of events (optic nerve damage/visual loss) but it is preceeded by pathological or physiological alterations.

STAGE : 2

Tissue changes which preceeds but may eventually lead to alterations in aqueous humor dynamics and optic nerve head function.

STAGE : 3

Functional alterations and physiological abnormalities leading to optic nerve damage.

STAGE : 4

Loss of axon as a result of events in stage2 and stage3

STAGE : 5

Vision loss due to nerve fibre layer and axonal damage glaucomatous field loss.[1]

ANATOMY OF ANGLE ANTERIOR CHAMBER

The angle is bound at anterior side by the peripheral part of cornea, the trabecular meshwork, the anterior face of the ciliary body and posterior wall is formed by the iris. The scleral groove lies between the scleral spur posteriorly and anterior border ring of schwalbe's line anteriorly, which is occupied by canal of schlemm and trabecular meshwork.

TRABECULAR MESHWORK

It is a triangular structure, the apex of which blends with the termination of descemet's membrane and deep corneal lamellae. The base of the triangle is attached to the anterior surface of scleral spur, anterior surface of ciliary body and root of the iris. The scleral sulcus is converted in to a circular channel called schlemm's canal by the trabecular meshwork.

Histologically it is composed of lamellae, made up of a central core consisting of ground substance collagenous and elastic like fibres, surrounded by a single layer of endothelial lining that is supported by a basement membrane. The anterior part of meshwork is non filtering and posterior filtering part is divided in to 3 portions.

1. UVEAL MESHWORK:

This portion adjacent to the anterior chamber are arranged in bands that extend from the iris root and ciliary body and extend to the peripheral cornea. This contains irregular openings ranging in size from 25-75 microns. This is the innermost part of the trabecular meshwork.

2. CORNEO SCLERAL MESHWORK:

This portion extends from the scleral spur to the lateral wall of scleral sulcus. The openings varying from 5 to 50 microns become progressively smaller as the schlemm's canal is approached.

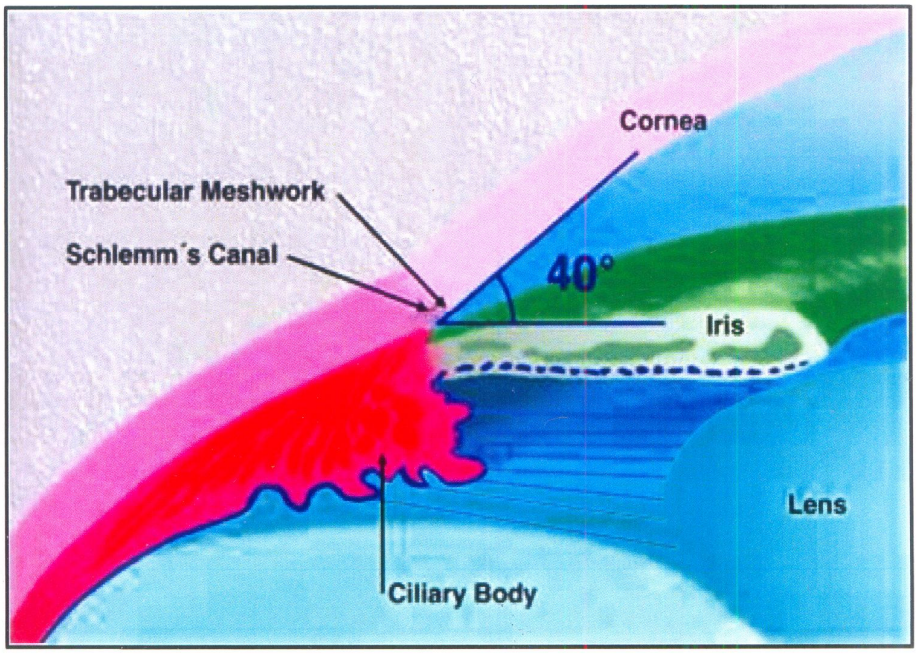
3. JUXTA-CANALICULAR TISSUE:

It is a thin layer of tissue 2-20 microns thick, the outermost portion of the meshwork adjacent to the schlemm's canal.

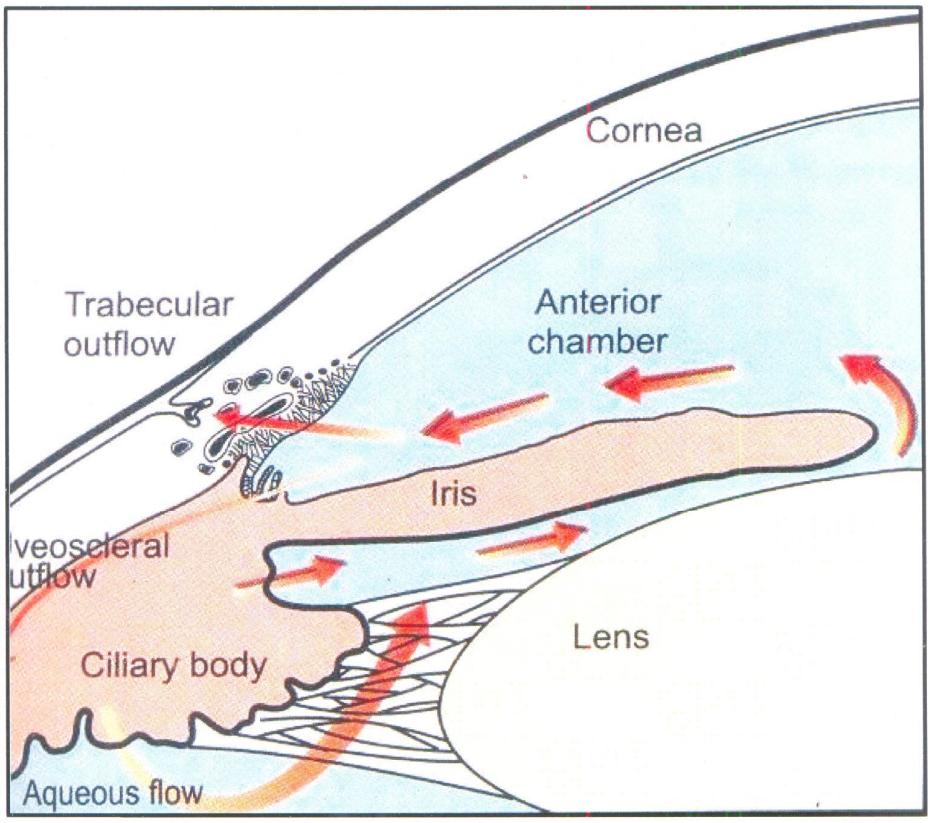
AQUEOUS VEINS

They are exit channels of aqueous first described by ascher. They vary in size from 0.01-0.1mm and interconnect schlemm's canal and episcleral veins.[1,4]

ANATOMY OF TRABECULAR MESHWORK



AQUEOUS OUTFLOW PATHWAY



INTRAOCULAR PRESSURE [IOP]

Normal intraocular pressure may be defined as the pressure that does not lead to glaucomatous damage of the optic nerve head. Unfortunately, such a definition cannot be expressed in precise numerical terms, in that all eyes do not respond the same to given pressure levels.

Three factors determine IOP :

- Rate of aqueous humor production
- Resistance to aqueous outflow across trabecular meshwork to schlemm's canal
- Level of episcleral venous pressure

FACTORS EXERTING LONG-TERM INFLUENCE ON IOP

1. GENETICS: The IOP within the general population appears to be under hereditary influence, through a polygenic, multifactorial mode of inheritance.
2. AGE: There is an increase in IOP with age.
3. GENDER: IOP is equal between the sexes in the age group of 20-40 years. In older age groups, the apparent increase in mean IOP with age is greater in women.

4. REFRACTIVE ERROR: A positive correlation exists between IOP and both axial length of the globe and increasing degrees of myopia.

5. ETHNICITY: Blacks have higher IOP than whites.

FACTORS EXERTING SHORT-TERM INFLUENCE ON IOP

1. DIURNAL VARIATION:

The intraocular pressure is subject to cyclic fluctuations throughout the day. The reported mean amplitude of daily fluctuation ranges from approximately 3mm of Hg to 6 mm of Hg. An amplitude greater than 10 mm of Hg is generally considered pathological. Many people reach their peak pressures in the morning hours, but others do so in the afternoon, in the evening or during sleep. The primary clinical value of measuring diurnal IOP variation is to avoid the risk of missing a pressure elevation with single readings. The intraocular pressures are recorded 6 times during the day at 4 hourly intervals and the graph is plotted connecting all points.

2. POSTURAL VARIATION:

The IOP increases from sitting to the supine position with reported average differences of 0.3-6 mm of Hg.

3. EXERTIONAL INFLUENCE:

Prolonged exercise such as running lowers the IOP. Valsalva maneuver increases the IOP.

4. LID MOVEMENT:

Blinking has been shown to rise the IOP.

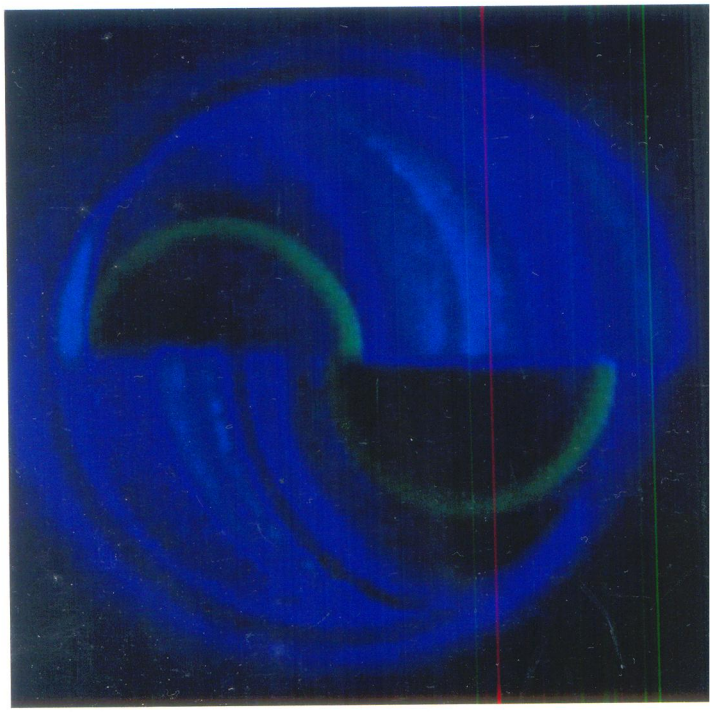
5. INTRAOCULAR DISEASES:

Anterior uveitis and retinal detachment are associated with a reduced IOP.

6. SYSTEMIC CONDITIONS:

Systemic hypertension and hyperthermia are associated with elevated IOP. The IOP has been reported to be lower with hyperthyroidism and higher with hypothyroidism. Diabetic patients have been reported to have higher IOP than the general population.

GOLDMANN APPLANATION TONOMETRY



7. ENVIRONMENTAL CONDITIONS:

Cold air reduces the IOP.

8. HORMONAL FACTORS:

Accumulation of corticosteroids topically, periocularly and systemically increases IOP. IOP varies with the menstrual cycle. It is low in the third trimester of pregnancy. Pharmacological doses of progesterones and estrogen reduced intra ocular pressure in experimental animals and man. Hormone replacement therapy in women has no effect on IOP. However esterified estrogen with methyl testosterone therapy does rise IOP.

9. GENERAL ANAESTHESIA:

It is usually associated with reduction in IOP. Drugs like ketamine and succinyl choline cause a transient rise in IOP.

10. OTHERS:

Alcohol and Heroin decrease the intraocular pressure whereas LSD and corticosteroids increase the intraocular pressure.[1]

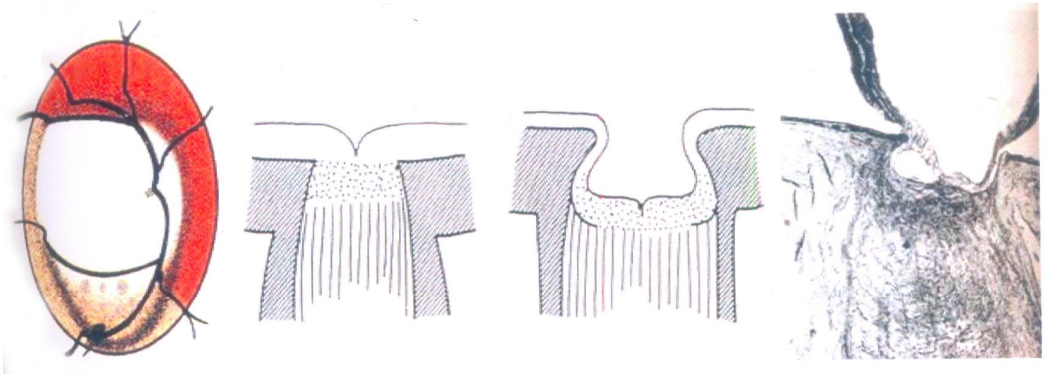
PATHOGENESIS OF GLAUCOMATOUS OPTIC ATROPHY

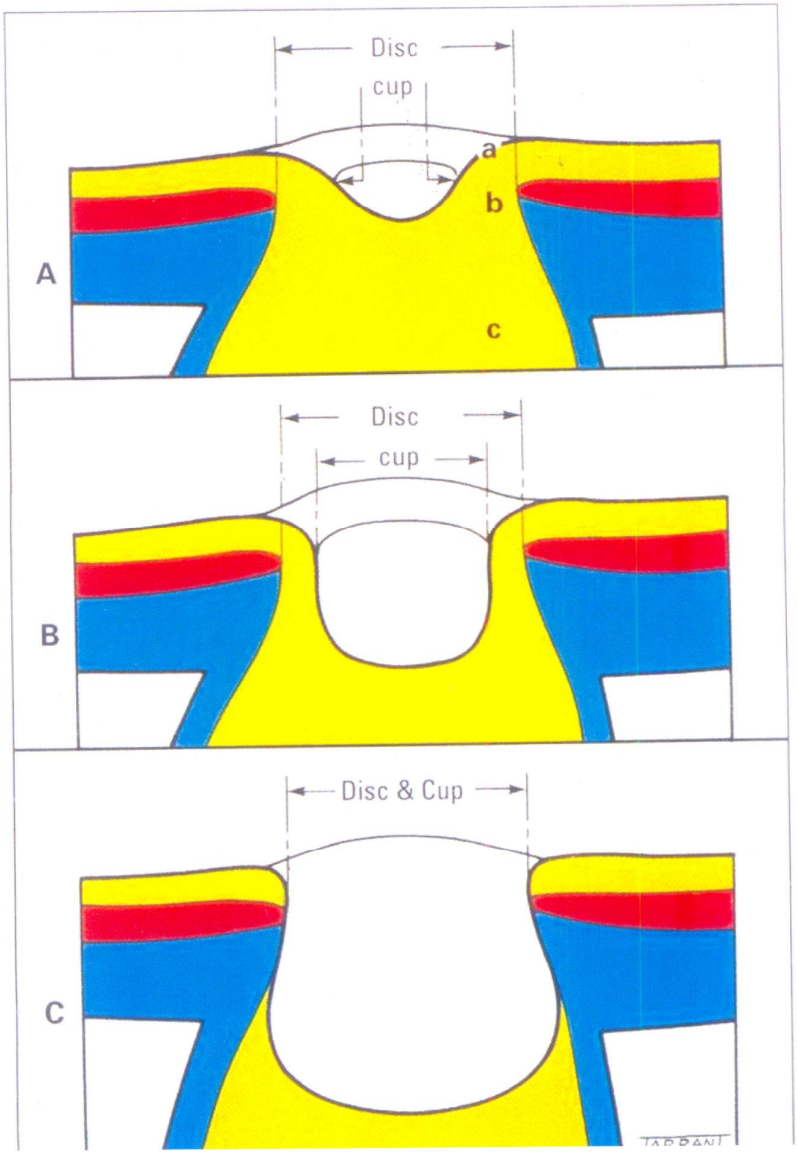
The pathogenesis of glaucomatous optic atrophy has remained the matter of controversy since mid 19th century.

The mechanical theory was proposed by Muller in which the elevated IOP led to direct compression and death of the neurons.

The vasogenic theory was proposed by Von-Jaeger. According to this theory the structural and functional defects occurring in glaucoma are due to ischemia. The most elaborate support for this theory was advanced by HAYREH. He proposed that both an increase of IOP and fall of blood pressure lead to fall of perfusion in the ocular vessels.

PATHOGENESIS OF OPTIC NERVE HEAD CHANGES IN GLAUCOMA





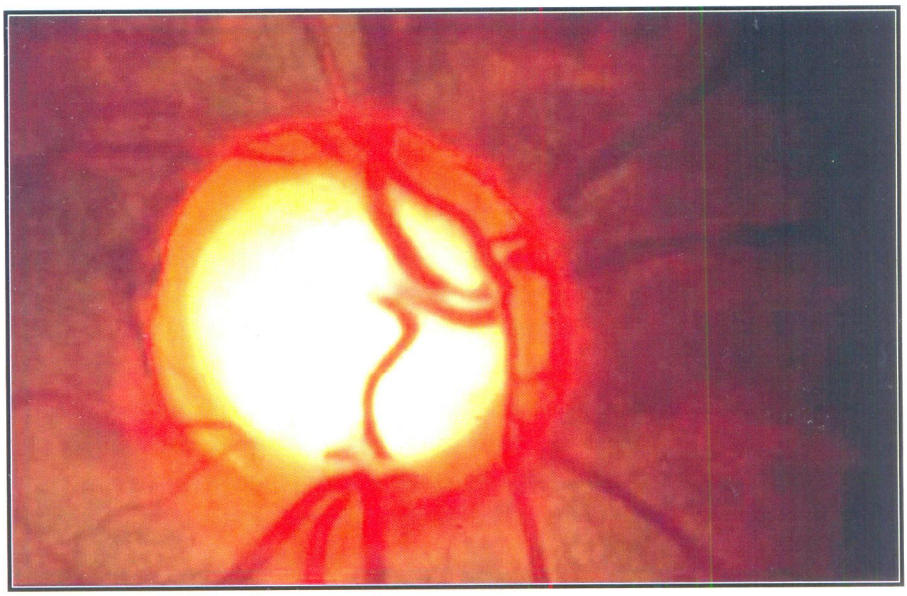
The fall of perfusion pressure can obliterate vessels first in the post laminar and retrolaminar region. The blood flow in the pre-laminar and post-laminar region and the choroid lack the ability of autoregulation. Optic cupping results from chronic ischemia of the optic nerve head.

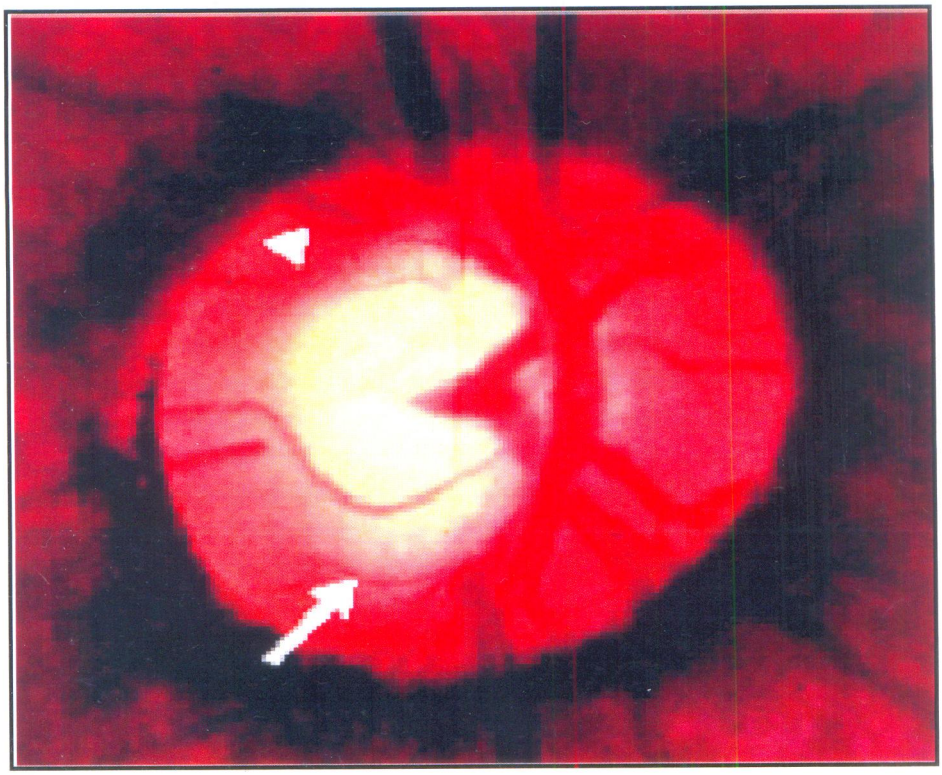
There are two weak points in the above theory. According to HAYREH the primary site of axon damage is the prelaminar disc area, but it has been found that it is actually in the lamina cribrosa region. There is evidence in favour of effective autoregulation of blood flow in the optic nerve head. Thus, Glaucomatous damage to the optic nerve is multifactorial and is affected by more than just IOP elevation.[1,2,5]

STRUCTURAL CHANGES OF GLAUCOMATOUS OPTIC ATROPHY

1. **FOCAL ATROPHY**
2. **CONCENTRIC ATROPHY**
3. **DEEPENING OF THE CUP**
4. **ADVANCED GLAUCOMATOUS CUPPING**

FUNDUS CHANGES IN GLAUCOMA





VASCULAR SIGNS OF GLAUCOMATOUS OPTIC ATROPHY

a. SPLINTER HEMORRHAGES

b. BARING OF THE CIRCUMLINEAR VESSEL

c. NASALISATION OF VESSELS

d. BAYONETING OF THE VESSELS

VISUAL FIELD LOSS IN GLAUCOMA

1. PERIPHERAL LOSS

2. LOCALIZED NERVE FIBER LAYER DEFECTS:

3. ARCUATE DEFECTS

4. NASAL STEP

5. EARLY GLAUCOMATOUS FIELD DEFECTS

a.Concentric contraction

b.Angioscotomata

6. ADVANCED GLAUCOMATOUS FIELD DEFECTS

a.Double arcuate scotoma

STEROID INDUCED GLAUCOMA

The response to long term Steroid therapy whether given by the topical, systemic procedure or intraocular route and the IOP elevation can lead to glaucomatous optic atrophy and loss of vision, such a condition is called as Steroid induced glaucoma.[1]

The clinical picture resembles that of chronic open angle glaucoma with an open normal appearing anterior chamber angle and absence of symptoms.

Approximately one third of the individuals experience moderate increase in IOP after topical steroid use. However 5-6% of normal population develops a marked increase in IOP after 4-6 weeks of topical steroid therapy. Thus 5% of the general population is considered to be “steroid responders” i.e they may develop steroid induced glaucoma when steroids are administered. This was shown by studies conducted by Armaly and Becker[13].

IOP Response to topical Corticosteroid administration

	Armaly	**Becker**
Frequency	QID	TDS
Duration	6 weeks	4 weeks
Parameter	Final IOP	IOP change
Type of responder	IOP mm Hg	IOP mm Hg
Low	< 20 (58%)	< 6 (66%)
Intermediate	20-31 (36%)	6-15 (29%)
High	> 31 (6%)	> 15 (5%)

ETIOPATHOGENESIS

Various theories has been put forth to describe the mechanism of steroid induced glaucoma

i. Nuclear transport of Glucocorticoid receptor :

Glucocorticoids have been shown to alter trabecular meshwork cell morphology by causing an increase in nuclear size and DNA content. Experiments on culture human trabecular meshwork cells exposed to dexamethasone have demonstrated that FK 506 binding immuno protein FK BP5, mediates nuclear transport of human glucocorticoid receptor GR Beta suggesting that this play a role in his increased glucocorticoid responsiveness.

ii. Influence on Extra Cellular Matrix :

Francois postulated that glycosaminoglycans in the polymerized form become hydrated, producing a biologic oedema that may increase resistance to aqueous outflow. Hyaluronidase in lysosomes depolymerise hyaluronate, corticosteroid stabilize the lysosomal membrane which may lead to an accumulation of polymerized glycosaminoglycans in the trabecular mesh work.

iii. Influence on Phagocytosis :

Endothelial cells lining the trabecular meshwork have phagocytic properties which may help to clean the aqueous of debris

before it reaches the inner wall of Schlemm's canal. Corticosteroid are known to suppress phagocytic activity and suppressed phagocytosis of the trabecular endothelium may allow debris in the aqueous to accumulate in the meshwork and act as barrier to outflow.

iii. Genetic Influences :

Multiple genes that may be involved in protective and damaging mechanisms with IOP elevation that are unregulated with dexamethasone (in addition to myocilin) α_1- antichymotrypsin, Pigment epithelium derived factor, cornea derived transcript 6, Prostaglandin D_2 Synthase, Growth arrest specific decorin, Insulin like growth factor binding protein – 2, Ferritin light chain, Fibullin-1C[1].

In an experiment involving exposure of cultured trabecular meshwork cells to dexamethasone, delayed increase in expression of a gene product was observed. This protein was termed as "trabecular meshwork inducible glucocorticoid response" protein initially localized to GLC1A locus on chromosome 1q 25, subsequently linked to the myocilin gene (MYOC).

MYOC gene spans approximately 17 Kb and contains three exons transcripting 2-3 kb gene product. Within the trabecular mesh work, it is equally expressed in the trabecular mesh work cells from the juxtacanalicular, corneoscleral and uveal layers. Normal myocilin expression increased in response to elevated IOP, dexamethasone

exposure and other forms of trabecular stress implying that it may have a protective role in outflow pathway. However recent study conducted in steroid responders failed to identify a statistically significant association between myocilin variations and steroid response[13].

Histopathology :

Light microscopy demonstrated accumulation of glycosaminoglycans that was best demonstrated by the Colloidal iron Stain, but was also seen with alcain blue.

Light microscopy revealed excessive accumulation of melanin pigment aggregates which were distributed through out trabecular meshwork involved juxta canalicular meshwork (JCM) and the endothelium lining Schlemm's canal.

The excessive pigmentation appeared to obscure the amount of acid mucopolysaccharide glycosaminoglycans (GAG). Endothelial lining of trabecular meshwork with Ruthenium red lining compared with control untreated eye. Electron microscopy showed an increase in glycosaminoglycans by Ruthenium red stain in the corticosteroid treated eye in contrast to control untreated eye.

Demonstration of acid mucopolysaccharide was confirmed in the tissue cultures of the trabecular meshwork in rabbit and pig eyes.

Electron microscopically glycosaminoglycans were identified using colloidal iron stain, this was demonstrated by Armaly and Wang

in Rhesus monkey, while Futa & Coworkers stained it in human trabecular meshwork.

Ruthenium positive deposits have been recently demonstrated in trabeculectomy specimen in chronic open angle glaucoma.

Rohen and associates described amorphous fibrillar material in the juxtacanalicular meshwork in two cases of glaucoma induced by topical administration of corticosteroids[45].

Glucocorticoid administration increases the expression of collagen elastin and fibronectin within the trabecular meshwork and induces expression of Sialoglycoprotein. Steroid use decreases expression of extracellular proteinases inducing fibrinolytic enzymes and stromolysin.

Ultra structural changes in the trabecular mesh work :-

The main finding in the steroid induced glaucoma is an accumulation of basement membrane like material staining for type IV collagen.

Glucocorticoids affect trabecular meshwork cell morphology by increasing synthesis of endoplasmic reticulum, golgicomplexes and secretory vesicles.Cell and nuclear size increases deposition of extracellular matrix and thickens the trabecular beams. This increases the expression of fibronectin and laminin.[5]

STEROID PROVOCATIVE TEST:

Steroid provocative test with dexamethasone was advised and tried. The pressure rose to 30 mm of Hg, visual field deteriorated substantially. After stopping steroid administration pressure remained elevated falling only to 21 – 27 mm of Hg. IOP does not fall to normal range. Post operative IOP correlates well with the level of serum hydrocortisone. Moreover a recent study has found a close relation between diurnal fluctuation of IOP and level of corticosteroid.

METHOD:

Topical dexamethasone 0.1% suspension was given to the right eye three times daily for a period of 4 weeks. At the end of 10 wks applanation tonometry was done.

PLASMA CORTISOL:

Hydro cortisone is a steroid hormone released in response to stress and low level of blood glucocorticoids. Its primary functions are to increase blood sugar through gluconeogenesis, suppress the immune system, aid in fat, protein and carbohydrate metabolism.

The amount of cortisol present in the blood undergoes diurnal variations, level peaks in the early morning (approximately 8 am) and reaches its lowest level at about midnight to 4am or 3 to 5 hours after the onset of sleep.

Plasma cortisol AM level:4.0 to 22 microgram/decilitre

Plasma cortisol PM level:3.0 to 17 microgram/decilitre

In steroid induced glaucoma patients plasma cortisol levels were rised both in the morning and night.

MECHANISM OF RISE OF IOP

An explanation for the apparently conflicting interpretations may be that corticosteroids may have biphasic effect. An increase in circulating corticosteroid may cause an increase in aqueous inflow whereas topical administration of this medication will produce a decrease in aqueous outflow. This differential effect may be atleast particularly a factor of vehicle used with topical medication, as several studies have implicated the vehicle as the agent which itself would be responsible for elevation of IOP.

The hypothesis that acute elevation of IOP may result from systemic administration of steroid and chronic glaucoma from topical usage was suggested by Grieten and Collignon Brach in 1965. Systemic corticosteroids have been observed to cause a rapid increase in IOP which fall quickly upon elimination of steroid.

In contrast, topically administered corticosteroids even in large doses does not seem to cause a pressure increase in period shorter than 1 week. The duration of administration may also play a role in determining the mechanism of elevation of pressure. As noted before the rise of pressure secondary to topical use of steroids requires several

weeks or more to develop. It may be, that the quicker type of response is related to an increase in aqueous inflow mediated by presence of hormone itself. In contrast, the more prolonged effect is a reflection of interference with aqueous outflow, perhaps due to structural alteration[45].

Routes of Administration :

i. Topical therapy :It occurs more often with topical therapy. fluorometholone 25% is less likely to increase IOP in corticosteroid responders.

ii. Periocular therapy – Periocular injection of a long acting corticosteroid is the most dangerous routes of administration from the stand point of steroid induced glaucoma.

iii. Intravitreal Therapy : Injection of triamcinolone acetonide increases the IOP by several mm of Hg in about half of the patients treated with 2 to 4 weeks after the start of treatment.

iv. `Placement of depot steroid implant in the vitreous has also been reported to produce serious elevation of IOP in large percentage of patients.

v. Systemic therapy: Systemic administration of corticosteroids is least likely to induce glaucoma.

ROUTES OF ADMINISTRATION LEADING TO STEROID INDUCED GLAUCOMA

Exogenous Corticosteroid:

Topical:

Ocular eye drops

Ocular Ointments

Inadvertent administration to eye from lids or face.

Periocular intravitreal injection

Systemic :

Oral

Injectable

Endogenous Corticosteroids

Adrenal hyperplasia

Adrenal adenoma

Ectopic ACTH Syndrome

After intravitreal triamcinolone, IOP rises in 50% of the eyes when compared with 1-2 months of injection of systemic corticosteroid. IOP rise was less with

i) Parenteral route

ii) Inhalational route of administration.

CLINICAL FEATURES :

Very few Symptoms exist

- History of use of steroids present
- History of systemic or ocular disease which could require chronic corticosteroid use (uveitis, collagen vascular disease, bronchial asthma).
- Age of the patient is important

  Infants may present with features of watering, photophobia, Blepharospasms, cloudy cornea, elevated IOP, Optic disc cupping like Buphthalmos, but unlike congenital glaucoma, angle of anterior chamber is normal.
- Teenager, adults presents features of primary open angle glaucoma.

Clinical evaluation reveals an elevated IOP, open and normal appearing angles on gonioscopy, painless white eye and optic disc cupping and visual field defects.

Steroid induced glaucoma may mimic low tension glaucoma when the Steroid induced pressure elevation has damaged the optic nerve visual field in the past, but IOP subsequently reduced to normal with cessation of steroid.

Steroid induced glaucoma may be masked following refractive surgery due to central corneal thinning, Ocular rigidity changes, Corneal oedema or fluid accumulation beneath Lasik flap.

Associated ocular finding from use of topical steroids include mydriasis, increased corneal thickness, corneal ulcers, posterior subcapsular cataracts, delayed wound healing, ptosis and skin atrophy of eyelids.

Eyes with vernalkeratoconjunctivitis (VKC) with and without glaucoma had similar corneal topography, increased IOP associated with steroid induced glaucoma and vernalkeratoconjunctivitis (VKC) may contribute to an increase in corneal curvature and posterior corneal elevation. Changes may be reversed by a reduction in the IOP with medical therapy.

Differential Diagnosis

1. Primary Open Angle Glaucoma
2. Uveitic Glaucoma
3. Glaucomatocyclitic Crisis
4. Normal tension glaucoma
5. Traumatic glaucoma (especially unilateral cases)
6. Juvenile glaucoma

MANAGEMENT :

1. Discontinuation of steroid use :-

   - Discontinuation of the use of steroid is the first line of treatment.
   - Stoppage of steroid normalises the IOP with in 1 to 4 weeks.
   - Acute resolution occurs in some cases within days of stoppage of steroid.
   - Duration of steroid therapy also appears to influence the reversibility to IOP elevation.
   - Administration of anti glaucoma drugs till IOP decreases to the normal level.
   - Lower potency drugs like fluorometholone, loteprednol, rimexolone, medrysone have lesser chances of increasing IOP.

2. **Excision of Depot Steroid :**

   - In all cases where depot steroid appears to be responsible for the rise in IOP, the optimal treatment if the medical management fails, is to excise the depot steroid.

- Topical steroids prescribed should be under the monitoring of an ophthalmologist.

3. **Glaucoma therapy :**

- Topical beta Blockers/aqueous suppressants

In eyes with steroid induced glaucoma due to Vernal Kerato Conjunctivitis prostaglandins should be avoided.

4. **Anecortave** acetate is a synthetic derivative of cortisol but very specific and irreversible chemical modifications to the cortisol structure have resulted in creation of a potent inhibitor of blood vessel growth with no evidence nonclinically or clinically of glucocorticoid receptor bioactivity.

   Anterior juxtascleral depot of AA (Anecortave Acetate) has been shown to lower IOP substantially in some eyes with medically controlled steroid related ocular hypertension.[13]

5. **Selective laser trabeculoplasty:**

   This is also used in the treatment of steroid induced glaucoma.

SELECTIVE LASER TRABECULOPLASTY

Selective laser trabeculoplasty is a new technology being introduced in the clinical practice of ophthalmology.

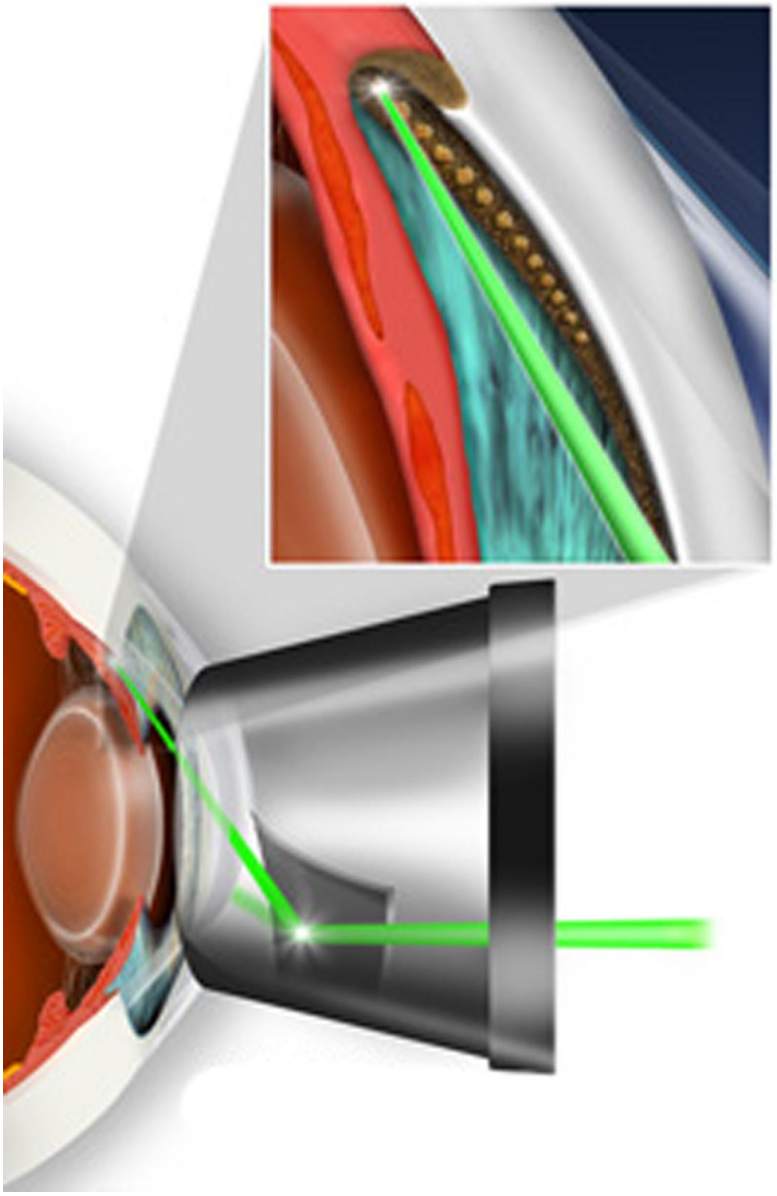
It was further developed by medical company (lumenis), with work done by Dr.Latina in 1995. SLT was introduced worldwide and it was cleared by the food and drug administration in march 2001. The key concept in the design of this laser system was to direct the energy towards only pigment containing cells in the trabecular meshwork.[12,20]

MECHANISM OF SELECTIVE LASER TRABECULOPLASTY

Dr.Jonge A.Alvarado of university of California, San Francisco explained the mechanism of Selective laser trabeculoplasty (SLT) and its practical implications.

Trabecular meshwork endothelial cells act as pressure sensors, when detecting increased IOP they secrete soluble factors namely cytokines into the aqueous humor. These cytokines induce longterm increase in permeability of schlemm's canal endothelial cells and thus the IOP is reduced.

SELECTIVE LASER TRABECULOPLASTY



When SLT irradiation is applied to the trabecular endothelium it recruits monocytes of the innate immune system. These cells in turn activate the trabecular endothelium cells causing the secretion of cytokines. These cytokines as shown microscopically increase the porosity of schlemm's canal endothelium thus reducing the IOP. It is likely that the monocytes also secrete cytokines which affect the porosity directly.[39]

It is effective for steroid induced glaucoma, reduces the mean intra ocular pressure by 30% more effective following intraocularpressure rise due to intravitreal triamcinolone.

Laser pulse duration is fixed at 3 nano seconds. The spot size is fixed at 400micrometre,which encompasses the entire meshwork from schwalbe's line to the ciliary body band. The laser energy is uniformly distributed to evenly treat the meshwork.

The power is adjustable from0.3 to 2.0 millijoule. The end point for the selective laser trabeculoplasty energy setting is the appearance of a tiny cavitation bubble and/or slight blanching of the trabecular meshwork. The energy can be increased from 0.6 to1.2milli joule.100 confluent applications were given per quadrant. It is usually performed for two quadrants (180 degrees) or for four quadrants (360 degrees) [20,21]

6. Trabeculectomy and glaucoma drainage device in uncontrolled glaucoma.

7. External trabeculotomy:

External trabeculotomy has been useful in treating steroid induced glaucoma. Fewer complications have been associated with this procedure. Various studies have proved the long time effect of this procedure on steroid induced glaucoma.[28]

STEROID INDUCED GLAUCOMA AND REFRACTIVE SURGERY

Steroid induced glaucoma is known to be masked following refractive surgery as IOP recordings are erroneous due to central corneal thinning, ocular rigidity changes, corneal oedema or fluid accumulation beneath the LASIK flap. Early onset steroid induced elevation of IOP after LASIK may cause corneal oedema and a sudden decrease in visual acuity. Rapid diagnosis and treatment can control IOP and recovers visual loss.

Steroid induced glaucoma has been reported after photo refractive keratectomy and is known to be under diagnosed for same reason.

PREVENTION :

i) Patient Selection :

Individuals with chronic open angle glaucoma and/or with the family history of the disease are more likely to respond to long term steroid therapy than other persons.

Patients with the following risk factors should be screened for glaucoma. The risk factors include myopic eyes, Diabetes mellitus, connective tissue disorder.

ii. Drug Selection :

When corticosteroid is required for any disorder, optimum drug is the one, that can achieve the desired therapeutic response by the safest route of administration in the lowest concentration and fewer potential side effects.

Careful monitoring of all patients on corticosteroid especially those with family history of glaucoma is warranted. Self medication and injudicious use of steroids should be avoided. If necessary steroid therapy must be used with intermittent drug holiday and never on continuous basis. [13]

PART TWO

AIMS OF THE STUDY

1. To analyse the clinical presentation and etiological risk factors in steroid induced glaucoma and duration and type of steroid used.
2. To establish the diagnosis and analyse about the management options in steroid induced glaucoma.
3. To know the response of selective laser trabeculoplasty in treatment of steroid induced glaucoma patients.

Inclusion Criteria

1. Patients with the history of steroid use either topically or systemically.
2. Persistent elevation of IOP more than 21mm of Hg or disc suspicious of glaucomatous damage.
3. Gonioscopically open angles.

Exclusion Criteria

1. Normotensive glaucoma
2. Narrow angle glaucoma
3. All other secondary glaucomas
4. Developmental glaucoma

Materials and Methods

The study was a prospective study conducted at glaucoma services at Regional Institute of Ophthalmology from the period between June 2009 – October 2011.

The study was done in 43 patients of established steroid induced glaucoma after complete evaluation.

A detailed history regarding the type of steroid used, mode of use, reason for use, and duration of use was recorded. The risk factors of family history of glaucoma, primary open angle glaucoma, Diabetes mellitus, hypertension, high myopia and connective tissue disorders were also asked in detail from the patients.

Patients were enquired about defective vision, defective field of vision and frequent change of glasses.

Visual acuity was recorded and refraction was done in all cases to correct refractive errors. Ocular examination of both eyes with slit lamp was done to rule out other causes of glaucoma and to know about the lens changes. Gonioscopy was done using single mirror Goldmann gonioprism and angles were graded by using shaffers grading method.

Intra ocular pressure was measured using Goldmann applanation tonometer and corrected to the central corneal thickness as measured by pachymetry.

Fundus examination was done using +90D slit lamp biomicroscopy and the cup, disc ratio was noted. Associated vascular signs like Nasalisation, Bayonetting, Laminar dot sign, Baring of circumciliary vessels and Splinter hemorrhages near the disc were noted.

Diurnal variation test (phasing) was done in all the patients by recording 6 readings each 4 hrs apart throughout the day plotting the graph connecting all the points. The recording was done using Perkins applanation tonometer.

Field charting was done by computer assisted static automated perimetry, (Octopus 123, G1X program TOP strategy) for both the eyes. Reliable field testing with false positives and false negatives below 30 percent were taken for the study.

Unnecessary usage of steroids was curtailed initially and the patients were followed up regularly. Certain patients with connective tissue disorders were on maintenance dose of steroids as advised by the rheumatologist. Patients were treated according to the amount of

glaucomatous damage. Then the patients were reviewed frequently and followed up regularly in equal intervals.

Plasma cortisol levels were measured at 8 am in the morning and 8pm in the evening for 10 patients.

Selective Laser Trabeculoplasty was performed for 10 patients. The patients who showed progress of glaucoma even after medical therapy were chosen for selective laser trabeculoplasty.

After selective laser trabeculoplasty patients were prescribed non steroidal anti Inflammatory drops and anti glaucoma drugs were continued for 5 days. Soon after which patients were reviewed, anti glaucoma drugs were stopped and evaluation was done after 2 weeks.

Blood pressure measurement done and hypertensives were referred to hypertension clinic.

Random blood sugar levels measured, if found high diabetologist opinion was obtained.

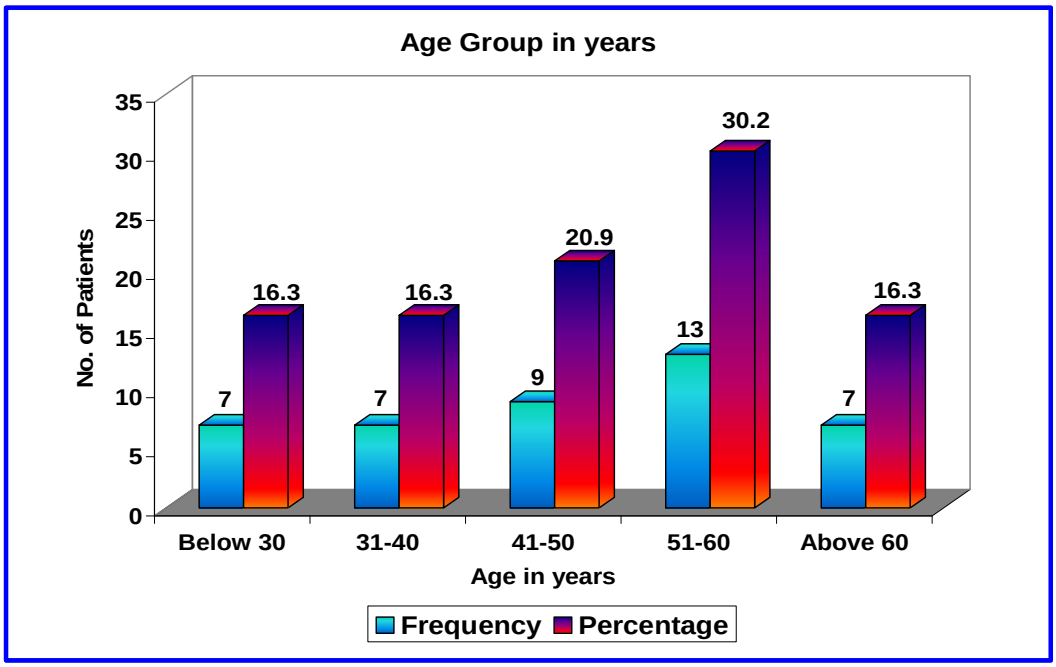
Patients diagnosed to have connective tissue disorders were under the care of Rheumatologist.

OBSERVATION AND ANALYSIS

68 eyes of 43 patients were taken into study. Two patients were one eyed. one had leucomatous corneal opacity and other patient had evisceration done in one eye. Rest of the 16 eyes were not involved. Steroid induced glaucoma resolved in 17 eyes of 13 patients with their stoppage of steroids and with initiation of medical treatment.

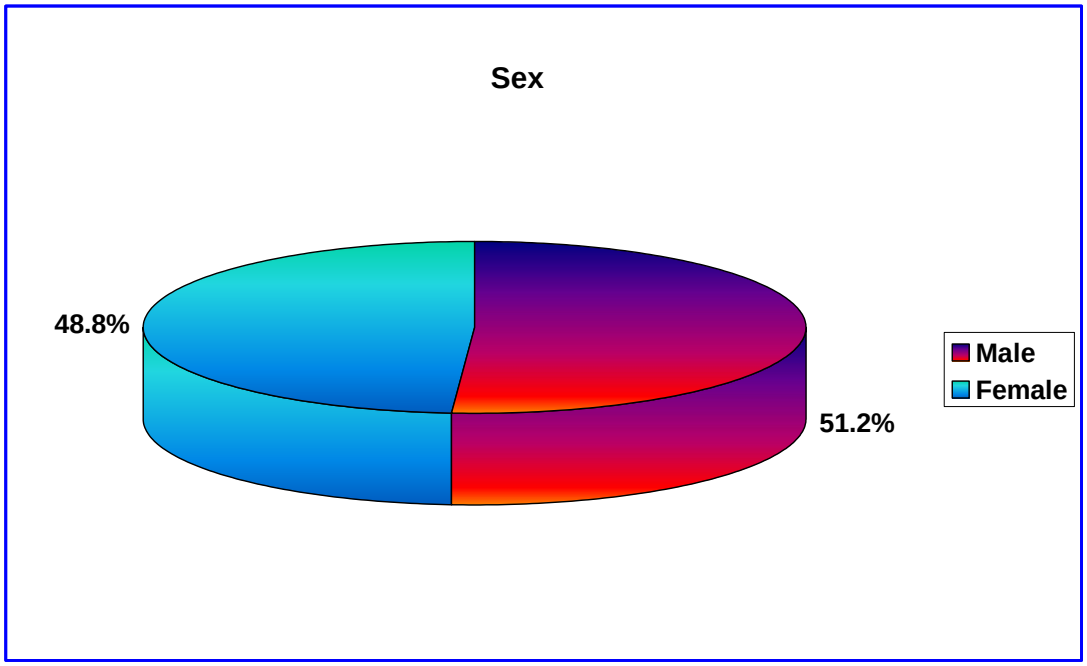
1. AGE DISTRIBUTION

Ages of the patients studied varied from14-65 years. There was no age preponderance. Predisposed patients were generally above the age of 40 years. The maximum age of incidence was between 51-60 years. Steroid use was more in older age groups for various medical ailments. This was similar to the studies conducted earlier[44].



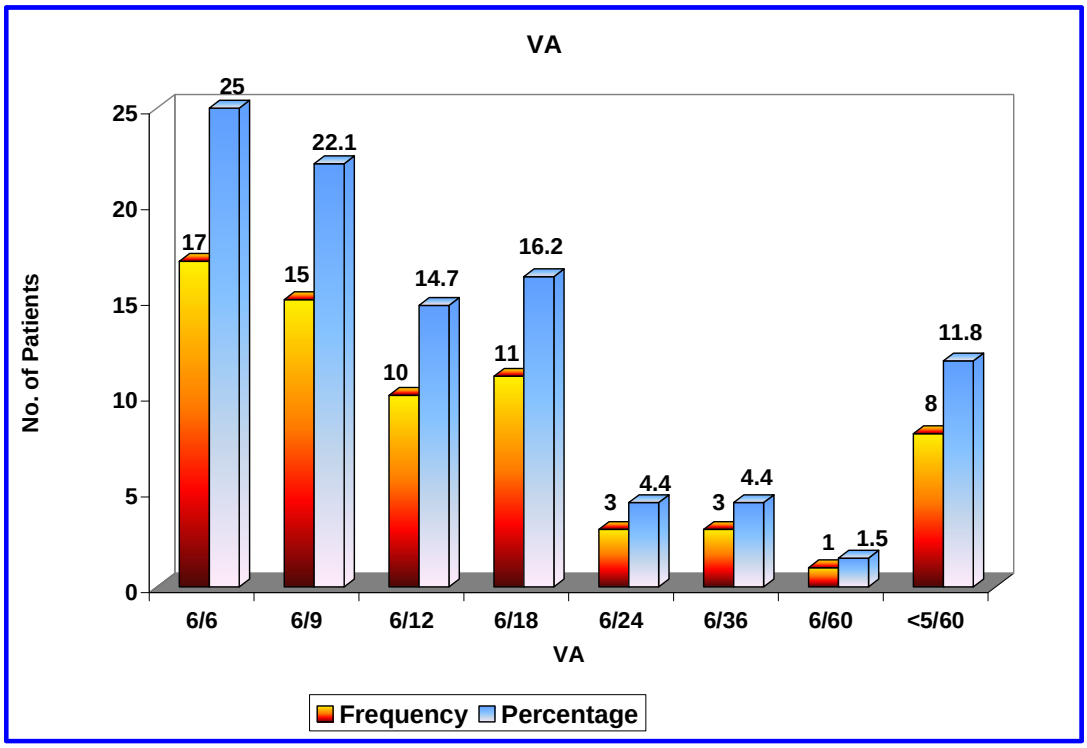
2. SEX

Among the 43 patients 22 were male and 21 were female. There was no sex preponderance. In the study group 51% were male 49% were female.



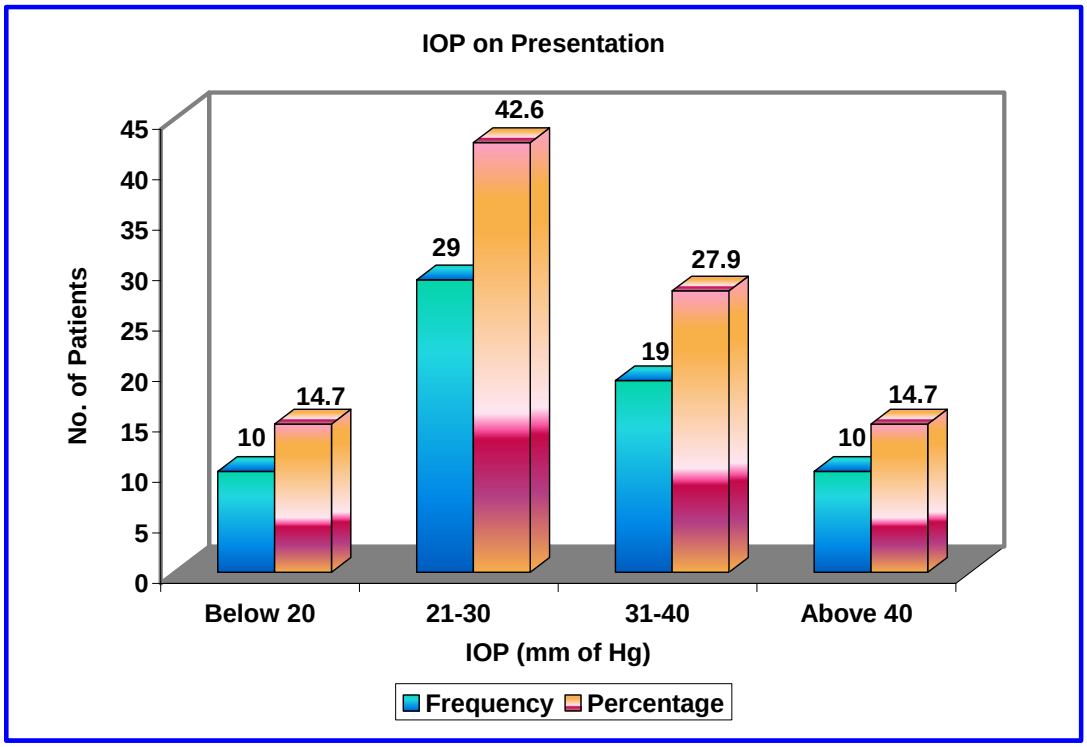
3. VISUAL ACUITY (VA)

Visual Acuity was normal (6/6) in 25% (17 eyes) of the cases. 8 eyes had vision less than 5/60 (11.8%).Among those 8 eyes, 1 eye had Posterior Capsular Opacification,2 eyes had severe posterior subcapsular cataract, 5 eyes had Glaucomatous optic atrophy. In 6(8.8%) eyes visual acuity was defective due to lens changes and in 37 (54.4%) eyes it was due to refractive error.



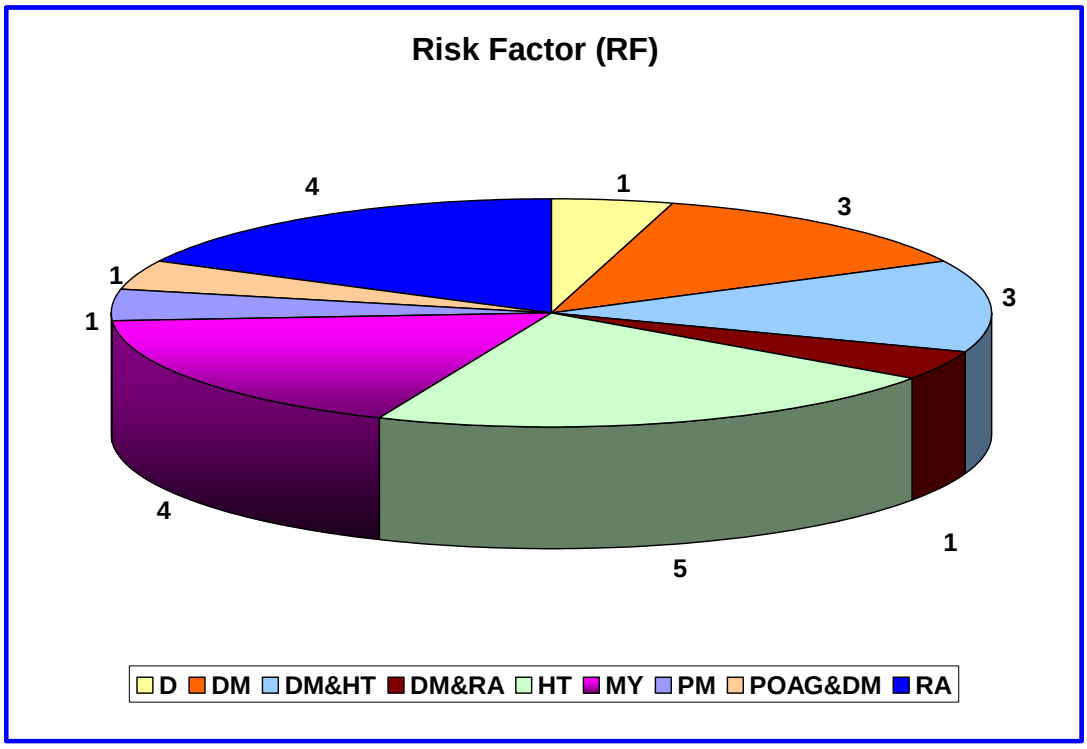
4. IOP DISTRIBUTION

Average IOP on presentation was between 21-30mm of Hg (42.6%) in 29 eyes. 10 eyes (14.7%) the IOP was below 20mm of Hg These patients had glaucomatous damage. They had already stopped applying steroid before presentation.IOP measured was similar to the previous studies.[44]



5. DISTRIBUTION OF RISK FACTORS

5 patients were hypertensives, 4 patients were Myope, 4 were case of Rheumatoid Arthritis, 1 patient had Diabetes Mellitus and Rheumatoid Arthritis, 3 patients had Diabetes Mellitus, 3 patients had Diabetes Mellitus and Hypertension, 1 patient had Primary open Angle Glaucoma and Diabetes Mellitus, 1 patient had dermatomyositis and 1 patient had polymyositis. Diabetes mellitus was the major risk factor in our study.This was similar to previous studies.[44]



D - Dermato Myositis

DM - Diabetes mellitus

HT - Hypertension

RA - Rheumatoid Arthritis

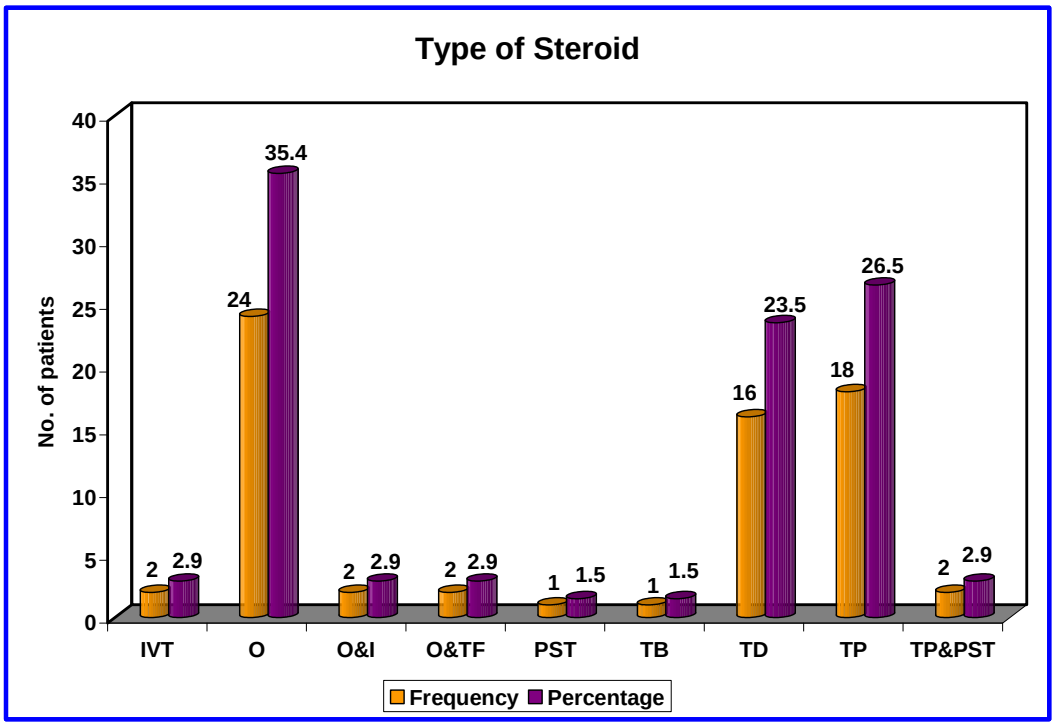
MY - Myope

PM - Poly Myositis

POAG - Primary Open Angle Glaucoma

6. TYPE OF STEROID USED

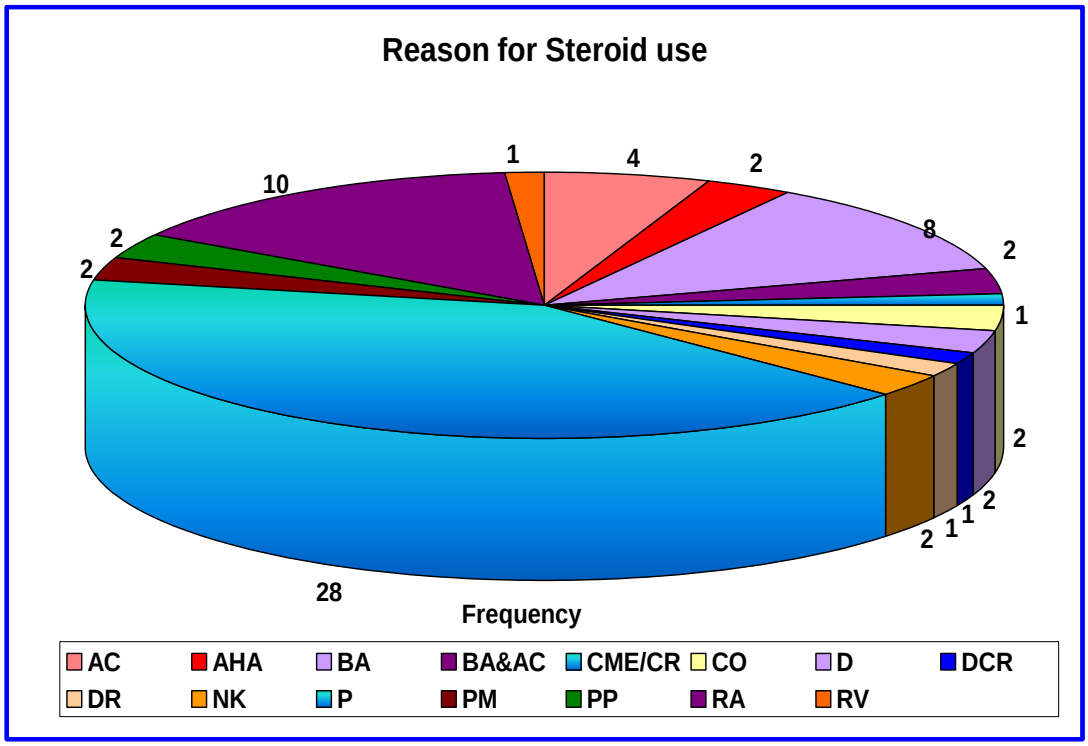
(41.2%) 14 patients (28 eyes) were on oral steroids.(4.4%) 3 patients had posterior subtenon injection.(2.9%) 2 patients intravitreal triamcinolone was given. (51.5%) 24 patients (35 eyes) were on topical medication alone. As per studies patients on topical medication are more prone for steroid induced glaucoma.[42,43]



IVT	-	Intra Vitreal triamcinolone
O	-	Oral
O & T	-	Oral and Injectable
O&TF	-	Oral and Topical Fluoromethalone
PST	-	Posterior Sub Tenon
TB	-	Topical betnesol
TD	-	Topical Dexamethasone
TP	-	Topical Prednisolone

7. REASON FOR STEROID USE

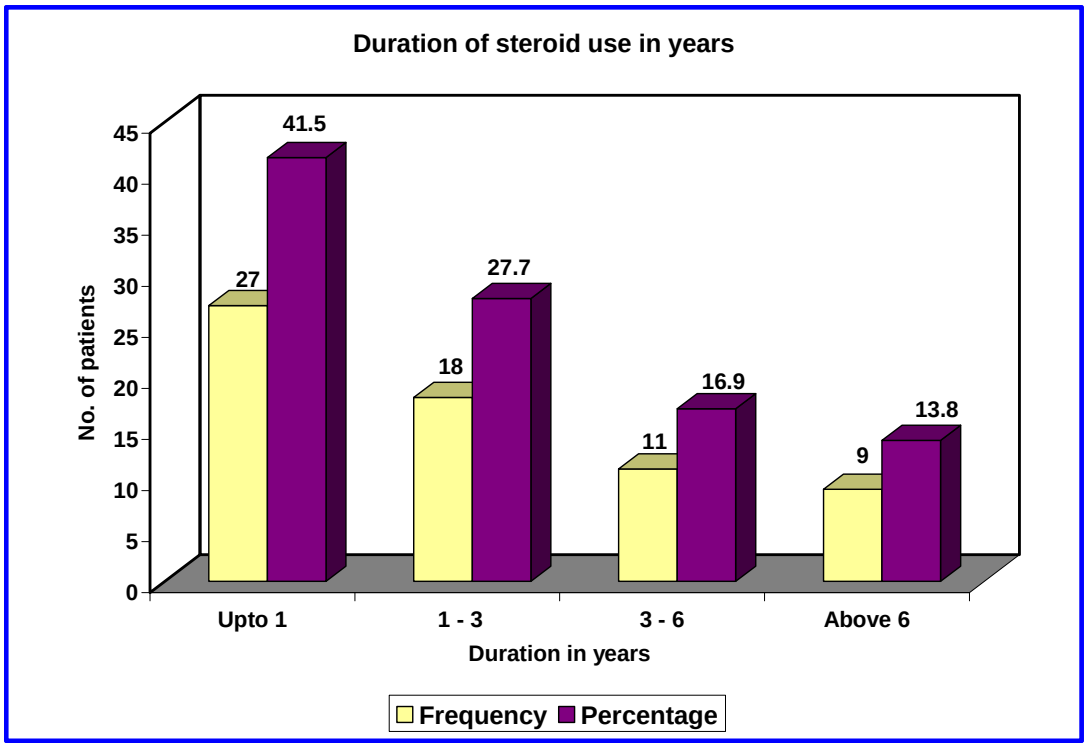
The most common reason for steroid induced glaucoma in our study was, following cataract surgery. 20 patients (41.2%) had under gone cataract surgery, of which 12 patient had undergone cataract surgery in only one eye. Rest 8 patients had undergone cataract surgery in both the eyes. As per studies done allergic conjunctivitis was the most common reason for steroid induced glaucoma.[42,43]



AC	-	Allergic Conjunctivitis
AHA	-	Autoimmune Hemolytic Anaemia
BA	-	Bronchial Asthma
CME/CR	-	Cystoid Macular edema due to central retinal Vein occlusion
CO	-	Chronic obstructive pulmonary disease
D	-	Dermato myositis
DCR	-	Dacro Cysto Rhinostomy
DR	-	Diabetic Retinopathy
NK	-	Nummular Keratitis
P	-	Post Operative
PM	-	Poly Myositis
PP	-	Pars Planitis
RA	-	Rheumatoid Arthritis
RV	-	Retinal Vasculitis

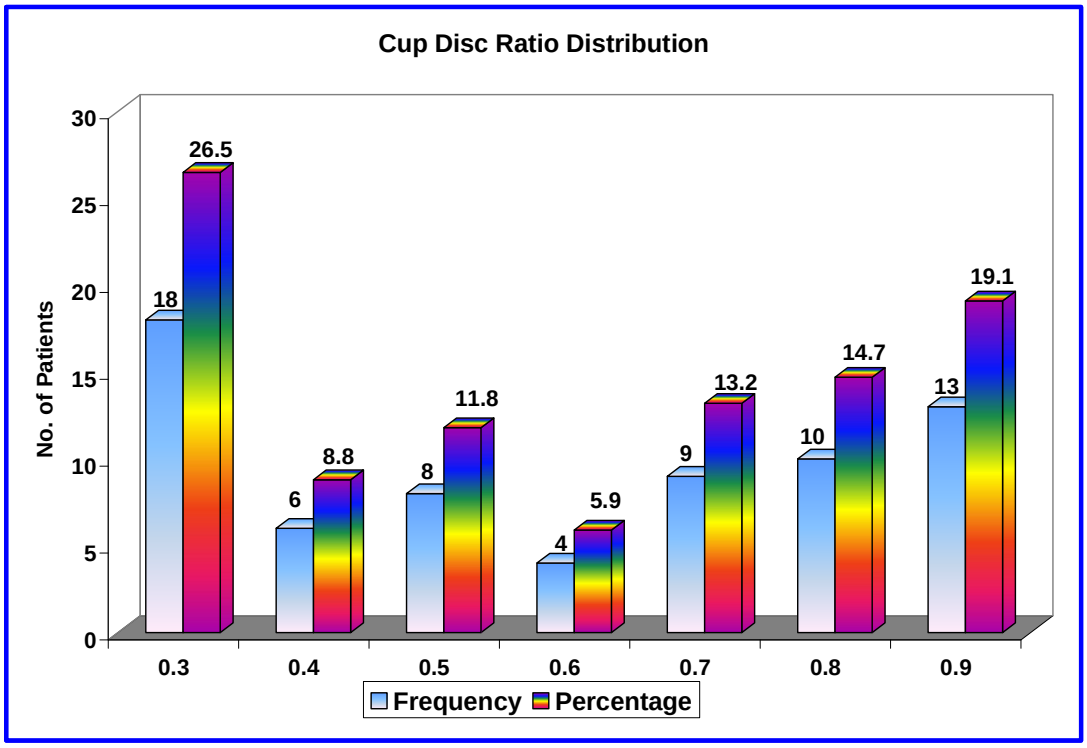
8. DURATION OF STEROID

Average duration of steroid in years, less than 1 year – 41.5% in 27 eyes and above 6 years (13.8%) in 9 eyes. For 2 Patients one dose of intravitreal triamcinolone was given, of which one was for cystoid macular edema due to central retinal vein occlusion, and for the another patient intravitreal triamcinolone was given for Diabetic Retinopathy. 3 patients were injected with posterior subtenon injection of which 2 were given for Parsplanitis and 1 for Retinal vasculitis.



9. OPTIC NERVE HEAD CHANGES

The average cup disc ratio was normal 0.3(26.5%) in 18 eyes.5 patients had glaucomatous optic atrophy

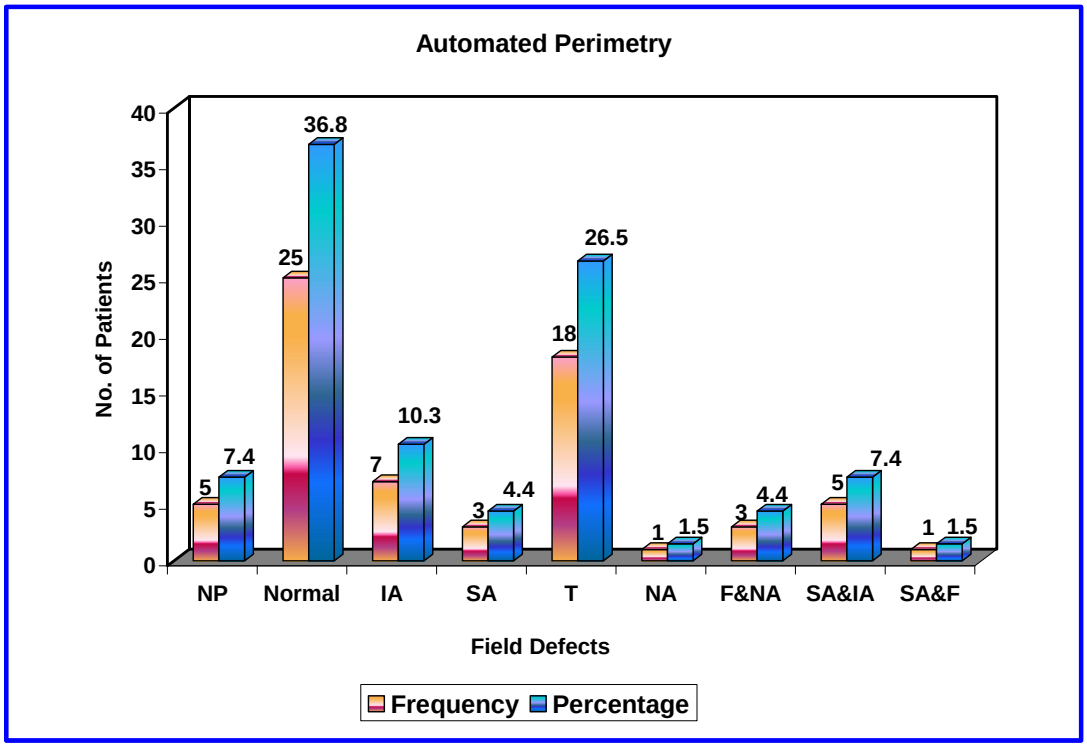


VASCULAR SIGNS

Fundus Findings	No. of Eyes	Percentage
Nasalisation of Vessels	48	70.5%
Bayonetting	32	47.1%
Laminar Dot Sign	46	67.6%
Baring of Circumlinear Vessels	6	2.9%
Splinter Hemorrhage	2	2.9%
Peripapillary Atrophy	24	35.3%

10. FIELD DEFECTS DISTRIBUTION

(36.8%) 25 eyes of patients in this study were found to be normal. 18 eyes had tubular field (26.8%), Inferior arcuate defects were found in 7 eyes (10.3%), Superior Arcuate defects were found in 3 eyes(4.4%). In 5 eyes (7.4%) Automated perimetry was not possible due to poor co-operation. Steroid induced glaucoma patients normally have field defects similar to Primary open angle glaucoma[1]



NP - Not Possible

IA - Inferior Arcuate defects

SA - Superior Arcuate defects

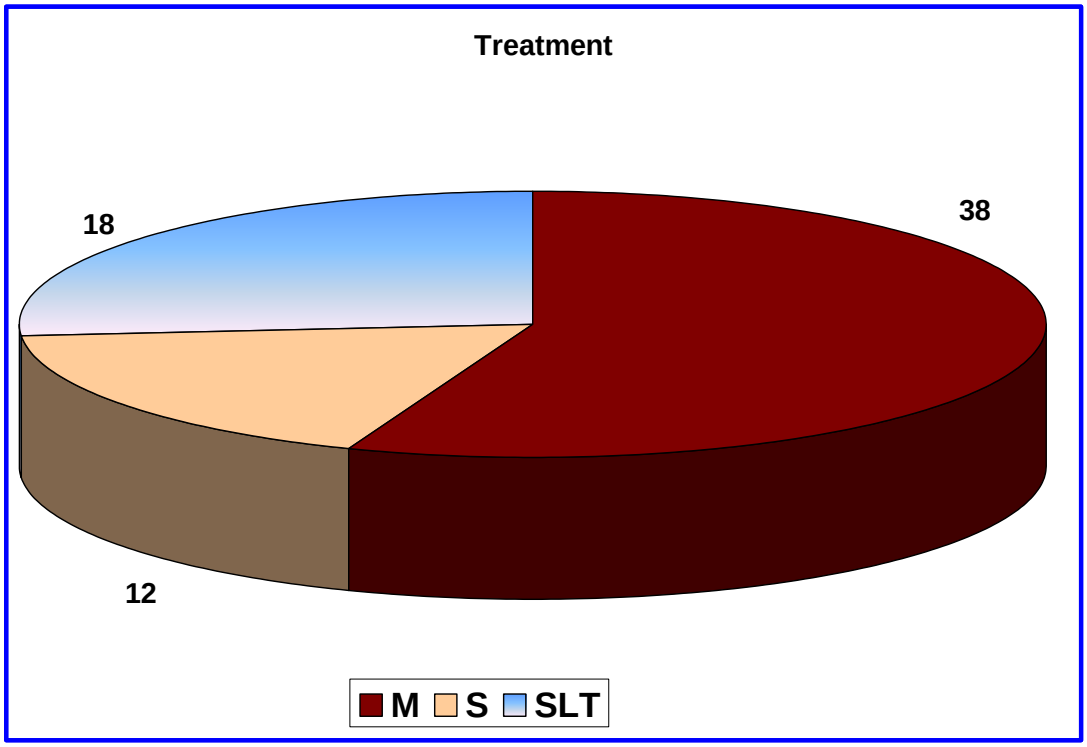
T - Tubular Field defects

NA - Nasal step defects

F - Fixation defects

11. TREATMENT

38 eyes had medical management of glaucoma. Depending upon IOP on presentation antiglaucoma medications were given. Based on Optic nerve head changes and follow up IOP (done after 3 weeks), antiglaucoma medications were either continued or stopped. Surgical treatment was done for 12 eyes, cataract extraction along with trabeculectomy was done for 7 eyes, Trabeculectomy alone was done for 5 eyes. Medical management followed by selective laser trabeculoplasty was carried out for 18 eyes.

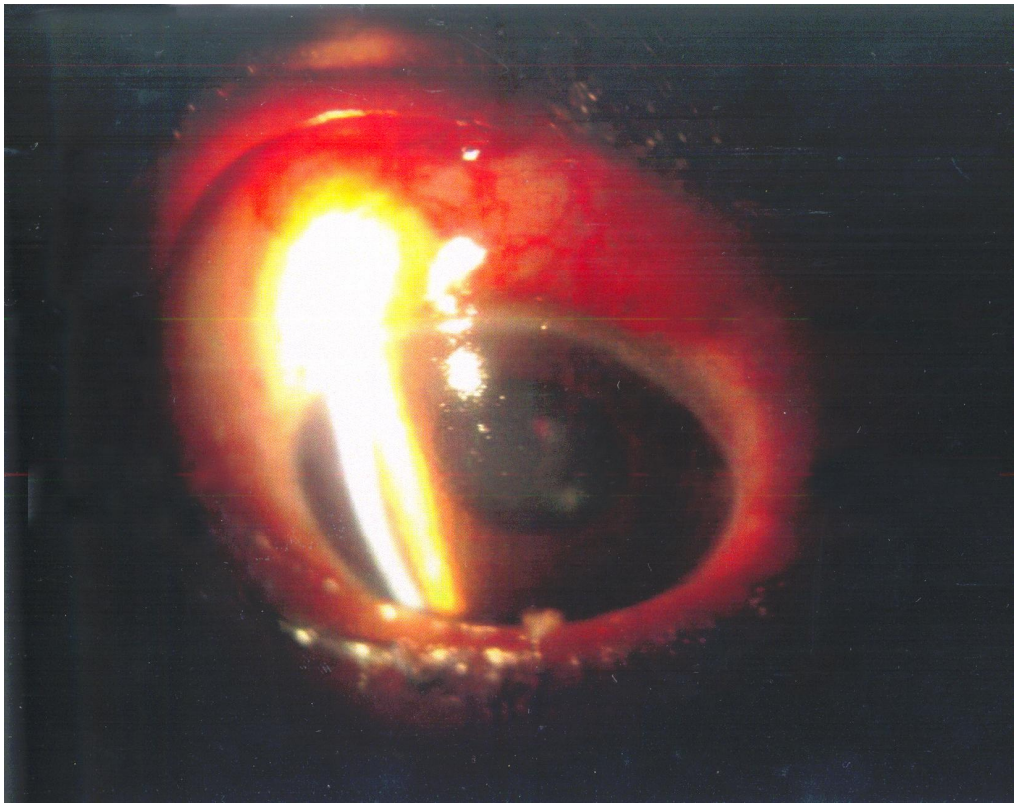


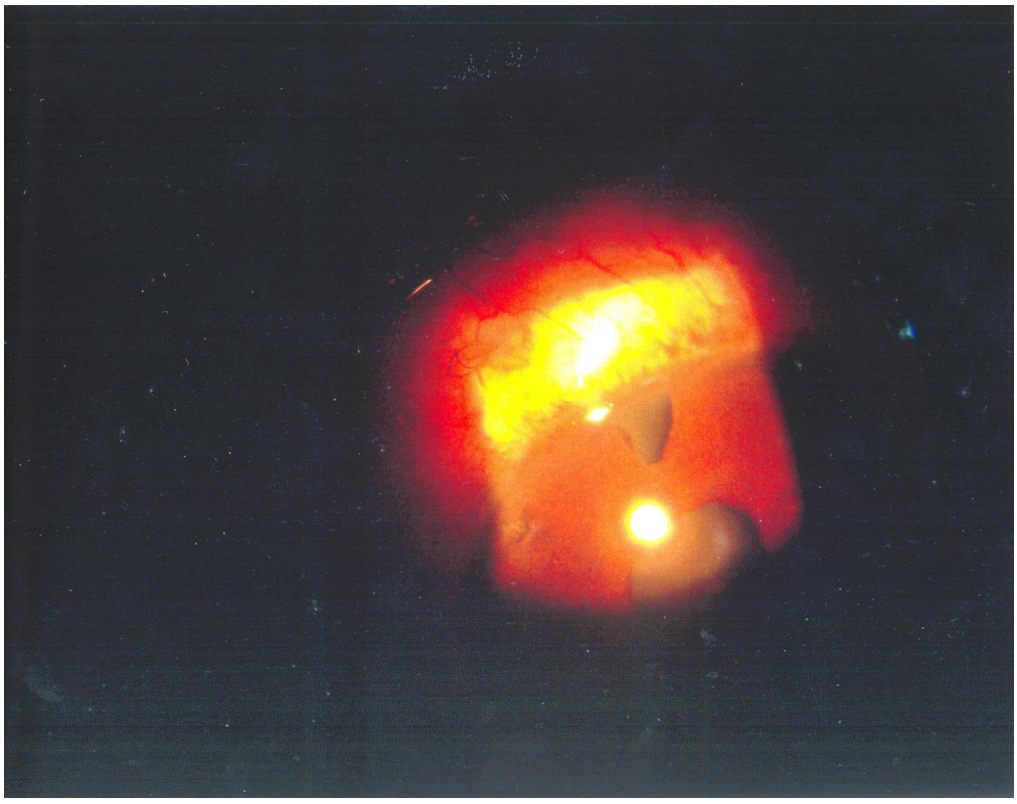
SLT - Selective Laser Trabeculoplasty and Medication

S - Trabeculectomy

M - Medication

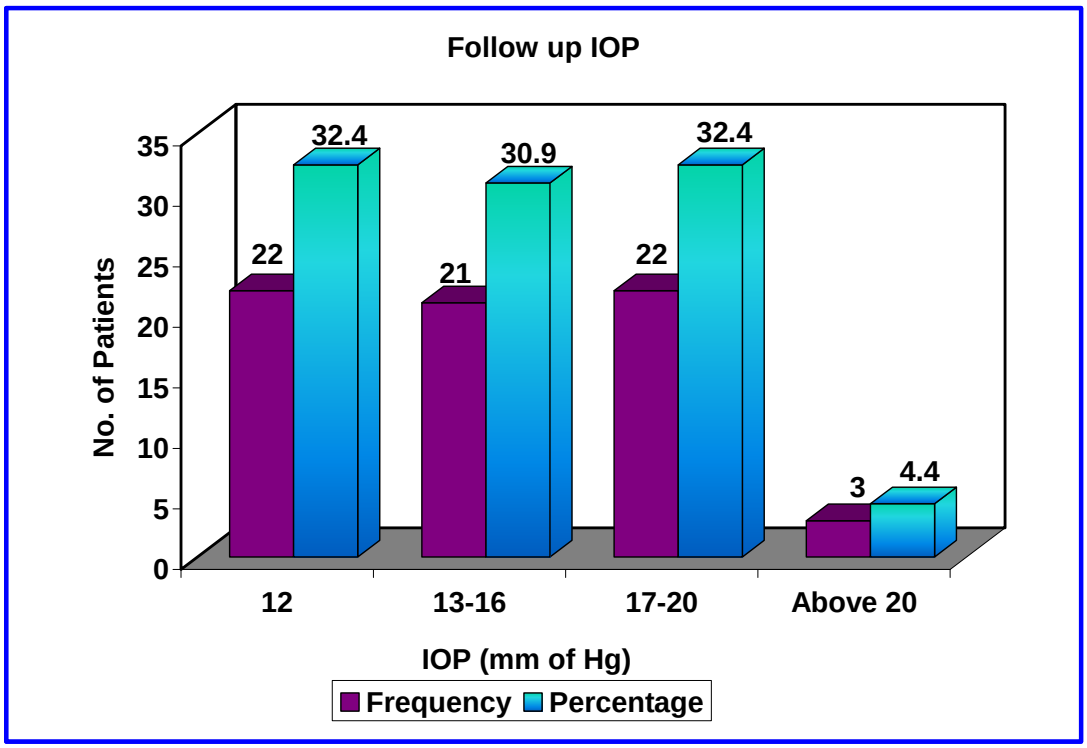
POST OPERATIVE PICTURE SHOWING FILTERING BLEB





12. FOLLOW UP IOP

The average follow up IOP was between 17 and 20 mm of Hg. In equal percentage of patients the follow up IOP was less than 12 mm of Hg. when the IOP on presentation was high (above 30), oral acetazolamide was given 250 mg BD, oral glycerol 30 ml TDS, intravenous injection of mannitol 200 ml BD, and topical medication of 0.5% BD timolol was given. Once the IOP was reduced medicines were gradually stopped or continued depending upon the glaucomatous changes.



13. STEROID INDUCED GLAUCOMA ALONG WITH CATARACT

14 eyes of 7 patients had post subcapsular opacity. 2 patients underwent cataract extraction with trabeculectomy. Lens changes were not compromised in of the 5 patients. Those who presented with cataract and glaucoma were all on oral steroids. Among the 7 patients, 3 patients had Rheumatoid Arthritis, 1 patient had Rheumatoid Arthritis and Diabetes mellitus. 1 patient was a case of Dermatomyositis, and 2 patients were Bronchial Asthmatics.

MAINTENANCE ON STEROIDS:

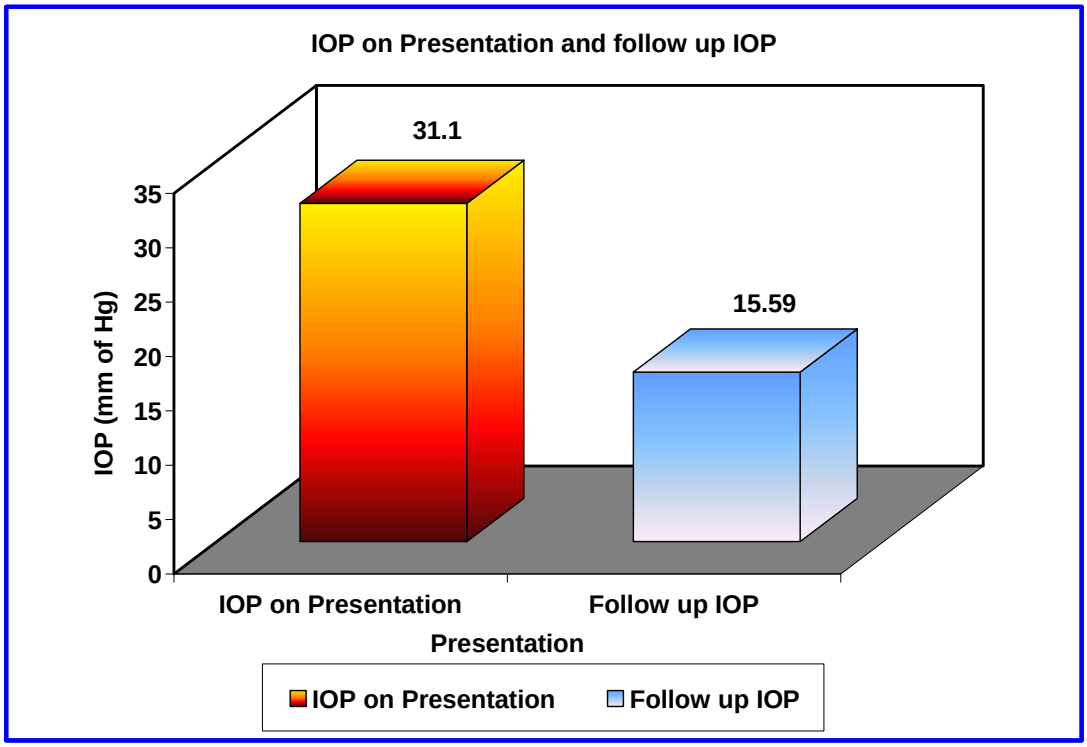
4 patients were on maintenance dose.3 patients of Rheumatoid Arthritis were on maintenance dose of tablet prednisolone. 1 patient of Dermatomyositis was also on maintenance dose of steroid. Selective laser trabeculoplasty has been performed for all these four patients and they are now on medical therapy. While 2 patients of Bronchial Asthma were on oral steroid only during exacerbation in winter season. Among these two patients surgery has been performed for one and the other patient is awaiting surgery.

DIURNAL VARIATION TEST

Once the diagnosis was made for Steroid induced glaucoma, Patients were started with medication, following which diurnal variation test was performed. In group I where 17 eyes of 13 patients were examined showed a mean diurnal variation of IOP as 3.1 mm of Hg In group 2 where 51 eyes of 30 patients were examined showed a mean diurnal variation of IOP as 5.4 mm of Hg. All the patients were followed up periodically. Disease progression was more in group 2 patients. Due to initiation of medication the mean diurnal variation of IOP was less than 10mm of Hg is both the groups.

14. COMPARISON OF IOP BEFORE AND AFTER TREATMENT

There was a significant difference in IOP before and after treatment. The values were compared by paired t test. The P value was <0.001, suggesting that the test is significant. The mean IOP on presentation was 31.10 mm of Hg and the mean follow up IOP was 15.59 mm of Hg.

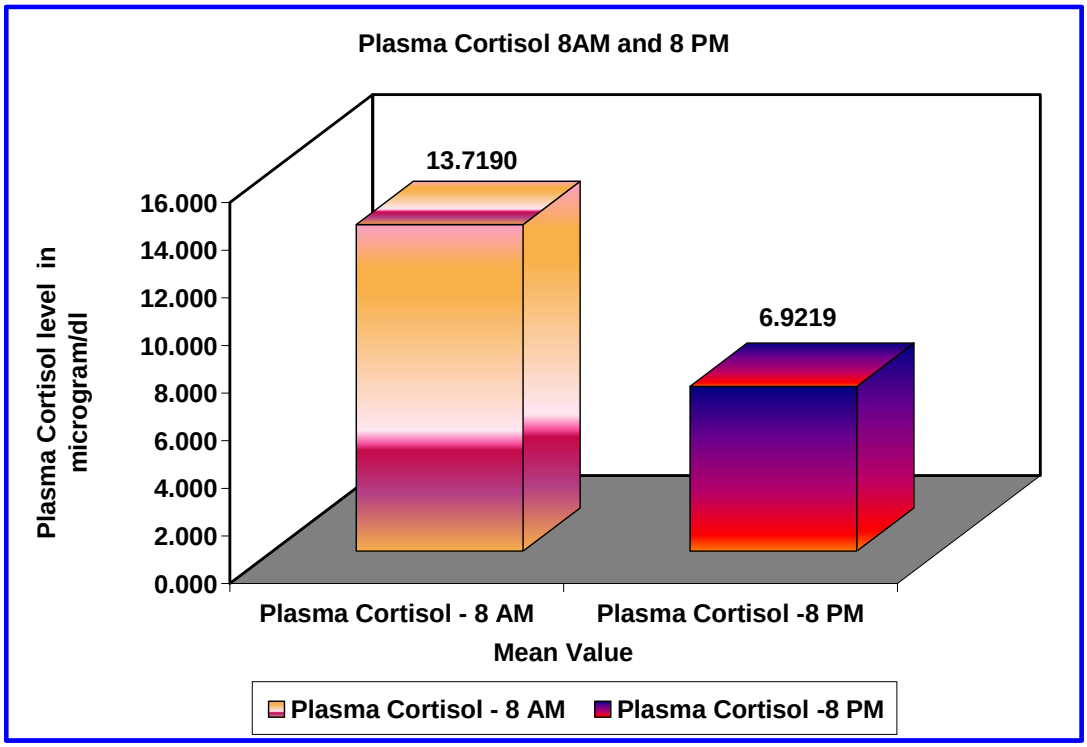


	Mean	**Standard Deviation**	**‘ P ’ Value**
IOP on Presentation	31.1	10.951	< 0.001
Follow up IOP	15.59	3.841	

NOTE: P value <0.001 denotes significance at 1% level

15. PLASMA CORTISOL

Plasma Cortisol levels were measured for 10 patients at 8 AM and 8 PM. The mean of values taken at 8 A.M in the morning was 13.7190. The mean of values taken at 8 p.m. was 6.9219. All the values found at 8 A.M. and 8 P.M. were within normal limits, showing that there is no effect of plasma cortisol in steroid induced glaucoma. Morning (8 A.M) values were greater than the evening (8 P.M) values. Morning (8 A.M) values compared with 8 p.m. (evening values) by t test showed significant variation with p value '0.012'.Plasma cortisol levels were not elevated because the patients in our study were already on medication when the test was performed.



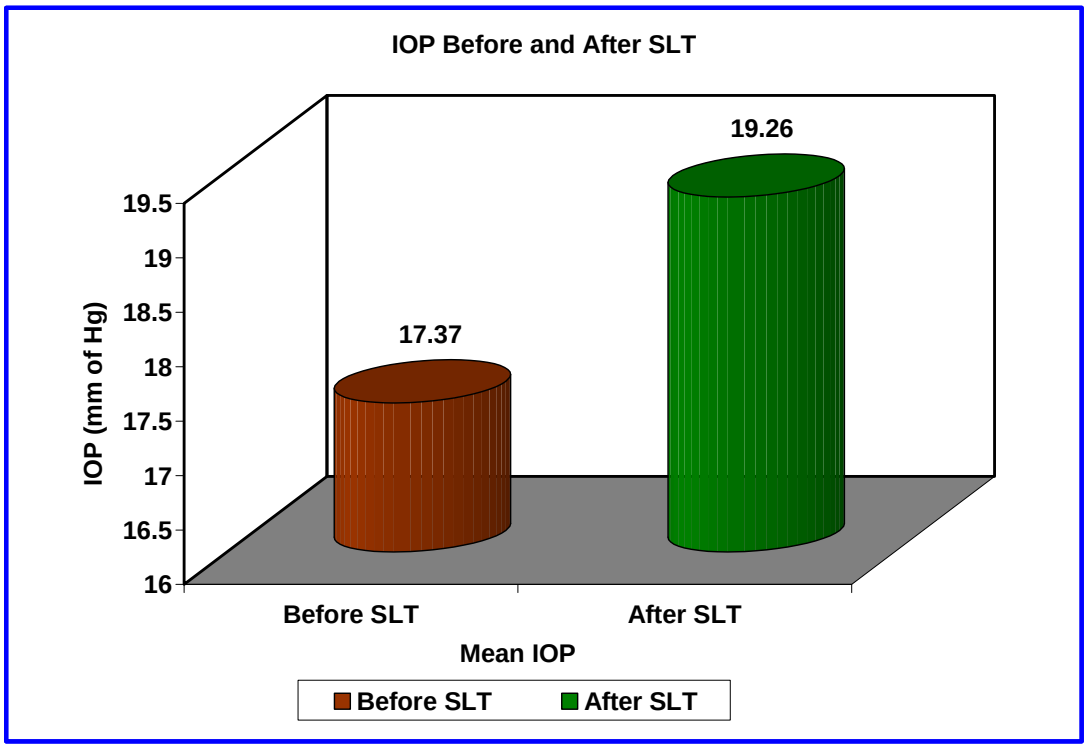
	Mean	**Standard Deviation**	**‘ P ’ Value**
Plasma Cortisol 8 AM	13.7190	6.00	0.012
Plasma Cortisol 8 PM	6.9219	3.90	

Note: P value of 0.012 denotes significance at 5% level.

16. COMPARISON OF IOP BEFORE AND AFTER SLT

The patients were treated medically with single drug before SLT. The aim of SLT was to provide benefit of reducing IOP similar to medication. So that patients need not apply topical medication.

The mean IOP before SLT was 17.37mm of Hg, the mean IOP after SLT was 19.26mm of Hg. This was because the antiglaucoma drugs were stopped three weeks in prior to the measurement of IOP. IOP of 18 eyes of 10 patients were compared with paired t test. P value was 0.283 suggesting that it was not significant. There by implying SLT did not bring down IOP to desired levels to prevent further disc damage. This was not consistent with the previous studies because, certain patients with connective tissue disorders were on maintenance dose of steroids, while others had advanced glaucomatous changes. These patients were followed up for a period of three months after SLT.



	Mean	Standard Deviation	' P ' Value
Before SLT	17.37	4.475	0.283
After SLT	19.26	5.086	

Note: P value of 0.283 suggest that it is not significant.

SUMMARY

- Steroid induced glaucoma resolved in 17 eyes of 13 patients with their stoppage of steroids and with initiation of medical treatment.
- The average age of presentation in the study was 51-60 yrs.
- There was no sex preponderance, males and females were equally affected.
- 17 eyes (25%) had normal vision 6/6 . 8 eyes (11.8%) had low vision less than 5/60.
- The average IOP at presentation was between 21-30 mm of Hg in 29 eyes (42.67%).The IOP was below 20 mm of Hg in 10 eyes (14.7%), 31-40 mm of Hg in 19 eyes (27.9%) and above 40 mm of Hg in 10 eyes (14.7%).
- The various risk factors in the study were diabetes melllitus, Hypertension, Rheumatoid Arthritis, Myopia. Diabetes mellitus constituted about 30% among the risk factors.
- 51.5% of patients were on topical medication alone.

- 41.2 % of patients developed steroid induced glaucoma following continued usage of topical steroid medication after cataract surgery.
- Two patients in our study who were given intravitreal triamcinolone had to undergo trabeculectomy, such cases were not seen in previous studies.
- Average duration of steroid use in years was less than 1 yr (41.5%).
- 13 eyes (19%) had cupping value of 0.9
- 18 eyes (26.5%) had CD ratio of 0 .3 .
- 48 eye (70.5%) showed nasalisation of the vessels and was observed to be the most common vascular sign.
- 18 eyes (26.5%) had tubular field.
- 25 eyes (36.8%)fields in automated perimetry was found to be normal.
- 38 eyes were treated with medication, 12 eyes were treated by surgical means, 18 eyes were treated with both medication and selective laser trabeculoplasty.

- The average IOP after treatment was below 12 mm of Hg in 22 eyes (32.4%) and between 17 and 20 mm of Hg 22 eyes (32.4%).
- 7 patients had posterior subcapsular cataract in both the eyes and all these 7 patients were on oral steroid therapy. 4 patients were still on maintenance dose of steroids.
- In the diurnal variation test 17 eyes of 13 patients showed a mean IOP of 3.1 mm of Hg.Glaucoma resolved in these patients with stoppage of steroid.
- There was a significant difference in IOP before and after treatment by medical or surgical means.
- plasma cortisol levels doesnot show any correlation in steroid induced glaucoma
- Selective laser trabeculoplasty was not effective in controlling IOP unlike medical or surgical treatment.

DISCUSSION

Steroid-induced glaucoma is an iatrogenic secondary open angle glaucoma, with decreased trabecular outflow causing a rise of intraocular pressure.

An increase in IOP occurs in response to the local or systemic use of corticosteroids, but the response varies among individuals. IOP response usually takes 2 to 4 weeks after starting topical steroids, though rarely there can be an acute rise of IOP within hours in association with systemic use of steroid or adrenocorticotropic hormone (ACTH). If the ocular hypertension is of a significant magnitude, not recognized, and not treated, subsequent glaucomatous optic neuropathy can develop (that is, steroid-induced glaucoma) In vernal keratoconjunctivitis (VKC), steroid induced glaucoma is a common complication as patients require long-term therapy and steroids are often used to provide early relief of symptoms.

Recently, the popular use of intravitreal triamcinolone acetonide (IVTA) for subretinal fluid, macular edema, and adjunctive therapy in the treatment of choroidal neovascularization has led to an increased incidence of corticosteroid-induced ocular hypertension and glaucoma. In our study 2 patients were given intravitreal injection of

triamcinolone. One for diabetic retinopathy with macular edema and the other for macular edema due to central retinal vein occlusion. Both of them under went trabeculectomy due to increased IOP on presentation, as it could not be controlled with medication.

Pre-existing POAG, or a status of a first-degree relative with POAG are important risk factors for corticosteroid-induced ocular hypertension and glaucoma. Age may be a risk factor; increased risk appears to occur in a bimodal distribution peaking first at age 6. As one progresses through adulthood age may not be a factor until late adult-hood when the risk again rises. Finally, those with connective-tissue disease, type-1 diabetes mellitus, and high myopia should all be considered to be high risk, and prudent follow up and monitoring is mandatory during prolonged periods of corticosteroid use.

Evidence supports several independent potential mechanisms of increased resistance to the outflow of aqueous humor that can act synergistically to produce corticosteroid-induced ocular hypertension:

1. Accumulation of polymerized glycosaminoglycans in the trabecular mesh work from reduced availability of Iysosomal enzymes.

2. Suppression of phagocytosis by trabecular endothelial cells with resultant accumulation of trabecular debris and increased outflow resistance.

3. Genetic influences, with possible upregulation of myocilin, optineurin and other factors with resultant increase in aqueous outflow resistance.

Diagnosis of steroid-induced glaucoma requires a high index of suspicion and the questioning of patients specifically about their use of steroid eye drops, ointments, skin preparations, and pills. History should also include duration of steroid use, and family history of glaucoma. Complete ocular examination should be done including measurement of IOP, gonioscopy and optic disc evaluation. Fundus photographs and optic disc imaging are desirable for documenting progression, though not mandatory.

In individuals with an IOP more than 20% above their baseline measurement, or in those for whom there is clinical or functional evidence of damage to their optic nerve during or after treatment with corticosteroids any or all of the following may be necessary to reduce IOP.

1. Determine if steroid use (in any form) is truly needed, stop or taper steroids.
2. Reduce the concentration or dosage of the steroid.
3. Change to a steroid with a lesser propensity for IOP elevation (e.g. fluorometholone, loteprednol, or rimexolone)
4. Switch to a topical nonsteroidal anti-inflammatory drug (e.g. ketorolac 0.4%, diclofenac 0.1%)
5. Start antiglaucoma therapy.
6. Obtain baseline visual fields and/or optic nerve photography or peripapillary retinal nerve fibre layer measurements, if appropriate.

If the IOP is at alarming levels (> 50 mmHg, even in the case of an optic nerve that appears healthy), surgical intervention with either a tube or a filter may be appropriate. Four patients in our study had IOP greater than 50 mm of Hg on presentation. Now their IOP is under control with medication. Among these three had advanced glaucomatous cupping and they have been advised to undergo surgery and the remaining one patient had normal fundus findings. These surgeries are required in fewer than 2% of patients receiving an intravitreal injection. Surgeons should consider a vitrectomy or the

explantation of the steroid implant for patients who have received intravitreal injections or intraocular implants of a corticosteroid.

Close and regular monitoring of the IOP of patients treated with corticosteroids is required (especially those with a personal or family history of POAG or steroid-induced glaucoma). The frequency of IOP monitoring should match the patient's risk factors for steroid induced spikes in pressure as well as the medication's potency, dosage, route of administration, and half-life and the duration of treatment.

High-risk patients who receive intravitreal injections require examinations one day and one week after treatment and at least monthly follow-up examinations after the medication's cessation.[41]

CONCLUSION

- In susceptible individuals and persons with risk factors, steroids should be avoided or if required should be administered in smaller doses.

- As per our study patients who underwent cataract surgery were more affected due to continued application of topical steroids. Topical steroid application should be stopped once the eye is quiet. Alternatively post operative patients who are prone to glaucoma should be prescribed preferably with non steroidal anti inflammatory drugs. IOP should be measured regularly in these individuals.

- In cases of advanced glaucomatous damage surgery will be a better option.

- Plasma cortisol does not correlate clinically in steroid induced glaucoma patients.

- Selective laser trabeculoplasty is not effective in preventing further glaucomatous damage.

- Selective laser trabeculoplasty helps in short term control of IOP.

FUTURE SCOPE:

Selective laser trabeculoplasty can be used in short term control of IOP. It is useful in very old patients who are not amenable to surgery and for those who are not willing for surgery.

Plasma cortisol levels can be measured more frequently once in four hours to find out the association between plasma cortisol levels and steroid induced glaucoma. It can also be carried out in larger number of patients.

Steroid provocative test will help in identifying the high steroid responders in the general population. It can also be performed in patients for whom intravitreal triamcinolone has to be given.

Genetic studies may throw more light on the etiopathogenesis of steroid induced glaucoma.

PART THREE

BIBLIOGRAPHY

1. Shields Text Book of Glaucoma – 6th Edition 2011.
2. Becker – Shaffer's Diagnosis and Therapy of the Glaucoma 8th Edition – 2009.
3. Chander and Grant's Glaucoma L.Epstein Randr Allin Gham JOEL Shuma Fourth Edition 1997.
4. Clinical Anatomy of the eye 2nd Edition, Richards Snells Michel A.Lemp.
5. The Glaucomas – Concepts and Fundamentals Tarek M.E.D. George L.Spaeth.
6. Myron Yanoff – Jay Duker Ophthalmology, 2009.
7. Albert jakobiec's Principle and Practice of Ophthalmology, Third Edition,Volume 2,Albert,Miller,Azar blod.
8. Duke – Elder. Sir. Volume III, Glaucomas.
9. Parsons' Diseases of the Eye Twenty – first Edition, 2011.
10. Kanski – Clinical Ophthalmology, Sixty Edition, 2007.
11. 21st century glaucoma.

12. Lasers in ophthalmology-basic diagnostic surgical aspect a review by Franz Fankhauser, sylwia Kwasniewska, Mark latina and David H Gosiengfiao.

13. Journal of current glaucoma practice may-august 2009 tanuj dada, soman nair, munish dawan.

14. Ophthalmology 1980,87,240

15. Archives of ophthalmology 1963; 70 ;492

16. Congress report: clinical society of ophthalmology

17. Acta ophthalmolegica volume 68 issue February 1990

18. Archives of ophthalmology 1969; 81; 788

19. American journal of ophthalmology 1987 103:716

20. Journal of glaucoma July 2008 volume 17 issue 4

21. P Lanzetta, N Manchini, G Virgili, Immediate Intraocular pressure response to Selective Laser Trabeculoplasty French Journal of Ophthalmology, Jan.1999 83:29-32.

22. Latina MA, Sibayan SA, Shin DH Noecker RJ,Marcellino G, Q Switched 532 nm Nd Yag Laser Trabeculoplasty Selective Laser Trabeculoplasty Ophthalmology 1998 105, 2082 – 2090.

23. American journal of ophthalmology 1953 36:389

24. American journal of ophthalmology 1958 45:108

25. Intra ocular pressure elevation associated with inhalation Journal of ophthalmology 1995 102:177

26. Archives of ophthalmology 1980 98:1577

27. Journal of glaucoma 2009 9:483

28. American journal of ophthalmology trabeculotomy, June 2011.

29. Review of ophthalmology 2003 selective laser trabeculoplasty for glaucoma therapy.

30. Archives ophthal Chicago 70, 482, 1963

31. Archives ophthalmology Chicago 71636, 1964

32. Becker, Hahn KA American Journal Ophthal, 1964.

33. Becker, Mills DW, Arch. J. ophthalmology Chicago Covell 1963 (L) 1958 A.

34. Ann Outist Paris 187,805, 1954.

35. 1st Congress European Ophthal Society, Laval and Collins R.

36. 1955 American Journal Ophthalmology 39, 179 Lepie G.S. Gioteari R.

37. Linner & Trans Ophthal society, 7927, 1959.

38. Nicholas JP Arch Ophthal Chicago, (1964).

39. Alvarado JA,Latina MA, Damji LF, Katz, Lt. The Science underlying Selective Laser Trabeculoplasty Ophthalmology Management, June 2002.

40. Corticosteroids and intraocular pressure Bernard Becker MD, Donald W.Mills Arch Ophthal 1963, 70 (4) 500 – 507.

41. Jones R IIIrd, Rhee Dj. Corticosteroid induced ocular hypertension and glaucoma: A brief review and update of the literature. Curr Opin Ophthalmol. 2006; 17(2):163.

42. Mohan R, Muralidharan AR, Steroid induced glaucoma and cataract,Indian Journal of Ophthalmology 1989;37:13-16

43. Eye 2008 22,26-30;doi:10.1038/sj.eye.6702474

44. Eye 2006 20,407-416;doi:10.1038/sj.eye .6701895

45. Trans Am Ophthalmol.Soc 1977 75:353-381

PROFORMA FOR THE CLINICAL

ANALYSIS OF STEROID INDUCED GLAUCOMA

Name :

Age : Sex : Address:

Phone No:

Glaucoma No:

Presenting Complaint:

Defective vision:

Headache:

Frequent change of glasses:

RISK FACTORS:	Tick If yes	Duration	Treatment

Family History:

Diabetes Mellitus:

Hypertension:

High Myope:

Connective Tissue Disorder:

Primary open Angle Glaucoma:

Type of Steroid:

Route of Steroid:

Duration of use:

Reason for use:

Past History :

Previous history of intraocular Surgery

BP:

Ocular Examination

V/A (BCVA) RE LE

IOP:

CCT:

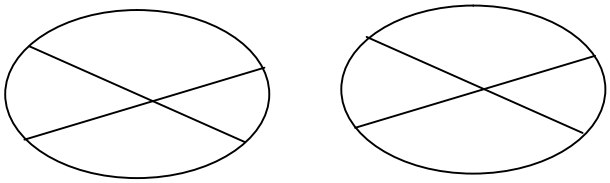
Anterior Segment:

Lens:

fundus :

Media :

C:D Ratio

Gonioscopy 

Automated
Perimetry:

Reliability :

Defects :

Diurnal IOP Monitoring:

Time	RE	LE

PlasmaCortisol(microgram/dl)

8 AM

8 PM

Blood Sugar(mg/dl):

Selective Laser Trabeculoplasty:

Pre laser IOP:

Post Laser IOP:

TREATMENT:

Medical

Surgical

Continuation of Steroids (if required):

Follow up:

Date :

Drugs :

Compliance:

Visual Acuity:

IOP:

Anterior Segment:

Fundus :

Automated Perimetry:

Advice:

LIST OF SURGERIES PERFORMED

1.	NATARAJAN	72/M	403061	19/8/09	LE IMC	LE ECCE with PCIOL
2.	SARADHA	70/F	57710	30/9/09	RE MC	RE ECCE with PCIOL
3.	MEGHANATHAN	61/M	447098	30/3/10	LE MC	LE ECCE with PCIOL
4.	JOHN	60/M	451362	4/8/10	RE IMC	RE SICS with PCIOL
5.	LAKSHMI	28/F	451619	14/8/10	LE UPPER LID CHALAZION	LE INCISION AND CURETTAGE
6.	ELUMALAI	65/M	423534	6/10/10	LE CHR.DAC	LE DCT
7.	MOHAMMED	46/M	4423122	18/10/10	RE PTERY CONJ	RE PTERY WITH AUTOGRAFT
8.	GOVINDAMMAL	67/F	455306	29/12/10	LE IMC	LE SICS WITH PCIOL
9.	RAGAMMA	50/F	456103	29/1/11	REPSCC	RE SICS WITH PCIOL
10.	SAHAYARAJ	55/M	456444	24/2/11	LE IMC	LE SICS WITH PCIOL
11.	LAVANYA	37/F	427833	18/3/11	RE CHR DAC	RE DCR
12.	SENTHIL	24/M	458125	2/4/11	LE PARTIAL THICKNESS LID TEAR	LE LID TEAR SUTURING
13.	LOGANATHAN	62/M	458709	26/4/11	RE IMC	RE SICS WITH PCIOL
14.	MUTHUAMMAL	55/F	459765	10/5/11	LE IMC	LE SICS WITH PCIOL
15.	MARUDHAAMMAL	60/F	460636	28/5/11	LE IMC	LE SICS WITH PCIOL
16.	SINTHAIYA	58/M	348872	2/6/11	RE PANOPH	RE EVISCERATION
17.	NAGAMMAL	70/F	461436	18/611	RELAGOPH	RE TARSORRHAPHY
18.	RANI	46/F	462611	2/7/11	RE PTERY	RE PTERY EXCISION WITH AMNIOTIC MEMBRANE

19.	PADMAVATHY	55/F	463571	13/8/11	RE IMC	RESICS WITH PCIOL
20.	SUBBRAYAN	60/M	463791	27/8/11	LEIMC	LE SICS WITH PCIOL
21.	SHANTHA	59/F	465267	1/10/11	LE IMC	LESICS WITH PCIOL
22.	KUMARESAN	65/M	423145	13/10/11	LE CORNEALTEAR	LE CORNEAL TEAR SUTURING DONE
23.	VELU	60/M	465838	22/10/11	RE IMC	RE SICS WITH PCIOL
24.	VEERASWAMY	66/M	466393	12/11/11	RE IMC	RE SICS WITH PCIOL
25.	CHETTU	65/M	466938	26/11/11	LE PSCC	LE SICS WITH PCIOL

ABBREVIATIONS

RE/LE	----------	**RIGHT EYE / LEFT EYE**
IMC	----------	**IMMATURE CATARACT**
MC	----------	**MATURE CATARACT**
PSCC	----------	**POSTERIOR SUBCAPSULAR**
CHR DAC	----------	**CHRONIC DACRYOCYSTITIS**
PTERY	----------	**PTERYGIUM**
CONJ	----------	**CONJUNCTIVA**
ECCE	----------	**EXTRA CAPSULAR CATARACT EXTRACTION**
SICS	----------	**SMALL INCISION CATARACT SURGERY**
PCIOL	----------	**POSTERIOR CHAMBER INTRA OCULAR LENS**
DCR	----------	**DACRYO CYSTO RHINOSTOMY**
DCT	----------	**DACRYOCYSTECTOMY**
PANOPH	----------	**PANOPHTHALMITIS**
LAGOPH	----------	**LAGOPHTHALMOS**

MASTER CHART

KEY TO MASTER CHART

Sl.No	Key	Description
1	M	Medication
2	TD	Topical Dexamethasone
3	TB	Topical Betnesol
4	TP	Topical Prednisolone
5	TF	Topical Fluorometholone
6	P	Post Operative
7	T	Tubular Field
8	DM	Diabetes Mellitus
9	SA	Superior Arcuate
10	IA	Inferior Arcuate
11	D	Dermatomyositis
12	L	Selective Laser trabeculoplasty
13	O	Oral
14	Na	Nasal
15	F	Fixation
16	RA	Rheumatoid Arthritis
17	N	Normal
18	My	Myope
19	BA	Bronchial Asthma
20	AC	Allergic Conjunctivitis
21	NV	No View
22	NP	Not Possible
23	PM	Polymyositis

24	S	Trabeculectomy
25	I	Injectable Steroids
26	PST	Posterior SubTenon
27	HT	Hypertension
28	HM	Hand Movements
29	CFCF	Counting Fingers
30	DR	Diabetic Retinopathy
31	IVT	Intravitreal Triamcinolone
32	CME	Cystoid Macular Edema
33	AHA	Auto Immune Haemolytic Anaemia
34	POAG	Primary Open Angle Glaucoma
35	DCR	Post Dacrocystorhinostomy
36	PL	Perception of Light
37	NO PL	No Perception of Light
38	PU	Pseudophakia
39	PSCC	Posterior sub capsular cataract
40	C	Lens clear
41	IM	Immature cataract
42	MC	Mature cataract
43	H	Phthisical eye
44	PP	Pars planitis
45	CO	Chronic obstructive pulmonary disease
46	RV	Retinal vasculitis
47	NK	Nummular keratitis

Sl.no	NAME	AGE	SEX	EYE	VA	IOP	CD	AP	RIsk Factor (RF)	TREATMENT	TYPE OF STEROID	DURATION	REASON	FOLLOW UP IOP	OCT (RNFL)	PLASMA CORTISOL		SLT BEFORE	SLT AFTER	LENS	CONT-STEROIDS
																8.00 AM micro gram/dl	8.00 PM micro gram/dl				
				RE	6/18 PH 6/12	48	0.4	NP		M	TD	2 Years	P	14						pu	no
1	Mr Desingu	51	M	LE	6/18 PH 6/12	42	0.5	NP		M	TD	2 Years	P	14						pu	no
				RE	PL	34	0.9	T	DM	M	TD	6 Years	P	18						pu	no
2	Mr Vincent	58	M	LE	6/60 PH 6/36	26	0.9	T	DM	M	TD	6 Years	P	16						pu	no
				RE	4/60	30	0.3	N		M	TP	4 weeks	P	16						pu	no
3	Mr Subramani	61	M	LE	6/6	16	0.3							14						pu	
				RE	6/6	24	0.7	IA	D	L&M	O	2 Years	D	18	89	1.02	6.449	16	16	pscc	yes
4	Mr Anand	36	M	LE	6/6	34	0.8	IA	D	L&M	O	2 Years	D	14	101			14	16	pscc	yes
				RE	6/36 PH 6/9	24	0.3	N	RA	L&M	O	9 Years	RA	12	12	10.7	2.02	16	22	pscc	yes
5	Mrs Lakshmi	47	F	LE	6/36 PH 6/9	34	0.3	N	RA	L&M	O	9 Years	RA	12	12			20	22	pscc	yes
				RE	6/60 PG 6/6	28	0.4	N	My	L&M	O&TF	2 Years	BA&AC	18	119	11.16	13.23	18	24	c	no
6	Mr Anand	27	M	LE	6/60 PG 6/6	35	0.4	N	My	L&M	O&TF	2 Years	BA&AC	26	106			20	26	c	no
				RE	1/2/60	14	NV	NP						14						h	
7	Mr Loganathan	55	M	LE	6/18 PH 6/12	32	0.3	N		M	TP	2months	P	12						pu	no
				RE	6/12 PH 6/9	16	0.3							16						im	
8	mrs.premalatha	52	F	LE	6/24 PH 6/18	24	0.3	N		M	TP	2 Months	P	18						pu	no
				RE	6/6	12	0.7	N	PM	M	O	2 Months	PM	12						c	no
9	Mr James	15	M	LE	6/6	12	0.7	N	PM	M	O	2 Months	PM	12						c	no
				RE	6/60 PH 6/24	34	0.8	SA IA		L&M	TP	8 Months	P	10				34	10	pu	no
10	Mrs Rani	50	F	LE	NO PL															h	
				RE	6/6	26	0.6	SA IA	RA	L&M	O	6 Years	RA	16		15.46	8.66	16	22	pscc	yes
11	Ms Devaki	46	F	LE	6/6	28	0.7	IA	RA	L&M	O	6 Years	RA	18				18	22	pscc	yes
				RE	5/60 PH 6/24	18	0.3							18						im	
12	Mr Kanniappan	75	M	LE	6/60 PH 6/18	34	0.3	N		M	TP	2 Months	P	16						pu	no
				RE	6/24PH6/12	28	0.4	N		M	TP	2 Months	P	18						pu	no
13	Mr abhimanyu	53	M	LE	6/12 PH 6/9	14	0.3							14						im	
				RE	5/60	14	0.8	T		S	O&I	15 Years	BA	14						pscc	yes
14	Ms Kumari	46	F	LE	5/60	14	0.8	T		S	O&I	15 Years	BA	14						pscc	yes
				RE	4/60 PH 6/9	30	0.3	N	My	M	TP&PST	2 Months	PP	10						c	no
15	Mr R.Selvaraj	14	M	LE	6/60 PH 6/6	16	0.3							16							
				RE	6/36 PH 6/9	28	0.6	N		M	TP	2 Years	P	16						pu	no
16	Ms Rajeswari	70	F	LE	6/36 PH 6/9	28	0.6	N		M	TP	2 Years	P	16						pu	no
				RE	6/9 PH 6/6	24	0.3	IA	DM	M	TP	6 Months	P	18						pu	no
17	Mr Kannan	45	M	LE	6/24 PH 6/18	30	0.3	F&Na	DM	M	TP	6 Months	P	20						pu	no
				RE	3/60 PH 6/60	14	0.3							14						im	
18	Ms Baby	61	F	LE	6/24 PH 6/9	60	0.6	IA	HT	M	TB	6 Months	P	20						pu	no
				RE	6/36 PH 6/18	42	0.8	T	HT	M	TP	2Years	P	18						pu	no
19	Ms Shantha	61	F	LE	CFCF	16	NV							16						im	
				RE	6/36 PH 6/12	28	0.9	T		M	TD	2 Years	P	12		10.84	2.16			pu	no
20	Ms Indhra	40	F	LE	5/60 PH 6/18	26	0.9	T		M	TD	2 Years	P	10						pu	no
				RE	6/18 PH 6/9	32	0.7	SA	RA	L&M	O	4 Years	RA	16		20.62	5.44	16	26	pscc	yes
21	Ms Vanaroja	55	F	LE	6/24 PH 6/12	32	0.7	SA	RA	L&M	O	4 Years	RA	16				16	26	pscc	yes
				RE	6/9 PH 6/6	10	0.3	N						10						pu	
22	Mr Saravanamuthu	57	M	LE	6/18 PH 6/6	34	0.3	Na	DM	S	IVT		DR	20						pu	no
				RE	3/60 PH 6/12	44	0.3	N		M	TP	6 Months	P	20						pu	no
23	Mr Sangaiah	43	M	LE	1/60	12	0.3	N						12						im	

				RE	6/12 PH 6/6	18	0.3	N						18						c	no
24	Mr Mohanraj	56	M	LE	6/60 PH 6/36	36	0.5	F&Na	HT	S	IVT		CME/CR	20						c	no
				RE	6/12 PH 6/9	56	0.3	N		L&M	TP	2 Months	P	12		21.76	4.06	16	20	pu	no
25	Mr Doss	60	M	LE	6/12 PH 6/9	58	0.3	N		L&M	TP	2months	P	12				14	24	pu	no
				RE	6/6	30	0.3	N	HT	M	O	2 Years	BA	18						c	
26	Ms Madhumathi	47	F	LE	6/6	24	0.3	N	HT	M	O	2 Years	BA	20						c	
				RE	6/60 PH 6/18	34	0.7	T		S	O	10 Years	CO	16						pu	no
27	Mr Mahalingam	60	M	LE	6/24 PH 6/12	24	0.7	T		S	O	10 Years	CO	12						pu	no
				RE	2/60	30	0.9	T	DM&HT	M	TP	2 Years	P	14						pu	no
28	Ms Meenakshi	65	F	LE	PL+	14	NV							14						mc	
				RE	6/9 PH 6/6	34	0.4	SA&F		M	TP&PST	4 Months	PP	20						c	no
29	Mr Anand	20	M	LE	6/6	18	0.3	N						18						c	no
				RE	6/60 PH 6/18	24	0.3	N	My	M	O	4 Months	AHA	16						c	no
30	Ms Abirami	25	F	LE	6/36 PH 6/18	26	0.3	N	My	M	O	4 Months	AHA	16						c	no
				RE	6/24 PH 6/18	34	0.9	T		M	O	3 Years	BA	10	70					pscc	yes
31	Ms Selvi	33	F	LE	1/60 PH 6/60	32	0.9	T		M	O	3 Years	BA	10	NP					pscc	
				RE	6/18 PH 6/9	24	0.8	T	DM&RA	S	O	2 Years	RA	10						pscc	no
32	Ms Kala	40	F	LE	1/60	34	0.9	T	DM&RA	S	O	2 Years	RA	12						pscc	no
				RE	6/60 PH 6/12	30	0.4	SA		M	TP	2 Months	P	20						pu	no
33	Mr Williams	48	M	LE	6/18 PH 6/9	16	0.3	N						16						im	
				RE	6/6	16	0.8	N		L&M	TD	10 Years	AC	16	105	12.64	6.09	18	18	c	no
34	Mr Abhijith	27	M	LE	6/6	18	0.8	N		L&M	TD	10 Years	AC	18	105			16	16	c	no
				RE	1/2/60	16	NV	NP						16						mc	
35	Ms Barammal	60	M	LE	2/60	48	0.9	T	HT	M	TD	2Years	P	24						pu	no
				RE	6/18 PH 6/9	28	0.5	N		L&M	TD	5 Years	P	18	104			18	16	pu	no
36	Mr Karnan	39	M	LE	6/60 PH 6/36	60	0.9	T		M	TD	8 Years	P	16	62					pu	no
				RE	6/24 PH 6/18	24	0.9	T	DM&HT	M	TD	7 Years	P	14						pu	no
37	Ms Hyrumbi	65	F	LE	6/18 PH 6/12	36	0.9	T	DM&HT	M	TD	5 Years	P	18						pu	no
				RE	6/36 PH 6/24	24	0.8	IA	POAG&DM	S	O	5 Years	BA	10						pu	no
38	Ms Madhu	60	F	LE	6/36 PH 6/24	24	0.8	IA	POAG&DM	S	O	5 Years	BA	10						pu	no
				RE	6/9 PH 6/6	20	0.3	N						18						c	
39	Ms Neelabai	55	F	LE	6/36 PH 6/18	60	0.7	SA&IA	DM&HT	M	TD	2 Years	DCR	26						c	no
				RE	NO PL	36	0.9	Np	RA	S	O	6 Years	RA	12						pu	no
40	Ms Lakshmi	49	F	LE	6/12 PH 6/9	24	0.5	SA&IA	RA	S	O	6 Years	RA	10						pu	no
				RE	6/6	30	0.5	NP		M	TD	4 Months	AC	12		18.43	12.78			c	no
41	Mr sargunan	17	M	LE	6/6	30	0.5	NP		M	TD	4 Months	AC	12						c	no
				RE	6/6	16	0.3	N						16						c	no
42	Ms kasiammal	35	F	LE	6/12 PH 6/9	40	0.3	N		M	PST		RV	20						c	no
				RE	5/60 PH 6/9	16	0.8	SA&IA	My	L&M	TP	6 Months	NK	12	109	14.56	8.33	12	10	c	no
43	mr rao	35	M	LE	5/60 PH 6/9	16	0.5	F&Na	My	L&M	TP	6 Months	NK	16	113			16	14	c	no